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References: Brit. J. Anaesth. *29*, 342

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"I would have everie man write what he knowes and no more."—MONTAIGNE

BRITISH JOURNAL OF ANAESTHESIA

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EDITORIAL

TREATMENT OF ACUTE RESPIRATORY INFECTIONS

THE paper by Drs. Nisbet and Wilson deals with a very old subject, "The Treatment of Acute Respiratory Infection in Infants". The authors begin by stating the sine qua non of efficient respiration where supply is equal to demand, the supply consisting of the two factors blood and oxygen. This is followed by the various causes of the failure of the oxygen supply and their treatment. As the main cause of oxygen deficiency is the accumulation of secretion, the removal of such secretion involves the often urgent use of mechanical means such as intubation, suction and possibly, where spontaneous respiration is still inefficient, by controlled positive pressure respiration. Assistant measures consist of the correct positioning of the patient, humidification of the atmosphere, suitable injections to liquefy sticky secretions, attention to the dressing and feeding of the infant and the countering of dehydration.

These writers so rightly stress that antibiotics, useful as they are, can be of no avail until the airway has first been attended to.

The case histories which follow show how these various remedies are applied; but, above all, what emerges is the necessity for the instant, always imminent, attendance of highly skilled and trained staff. Of the five deaths recorded three were attributed to respiratory obstruction, an obstruction that it is assumed could have been relieved if a trained attendant had been there in time.

It is obvious that such lives can only be saved by the establishment of a special department adequately staffed. As these children die quickly "adequate staffing" must mean the immediate availability of a highly skilled nurse or doctor at all times—a very large order. The training of the modern anaesthetist makes him a most useful member of the team, both in a supervisory and advisory capacity, as well, at a more junior level, as an on-the-spot executive. There is a great deal to be said for the establishment of such special units in each regional area in selected adult and paediatric hospitals.

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THE CARDIOVASCULAR EFFECTS OF HALOTHANE IN NORMAL CHILDREN

BY

M. McGREGOR,* H. T. DAVENPORT, W. JEGIER, P. SEKELJ, J. E. GIBBONS AND P. P. DEMERS

The Departments of Cardiology, Anaesthesia and Bio-Physics of The Montreal Children's Hospital and McGill University, Montreal, Canada

THE substance 1, 1, 1, trifluoro-2, 2 bromochlorethane was first introduced as an anaesthetic agent by Raventos (1956) and shown by him and others in several subsequent reports to have some highly desirable characteristics as an anaesthetic agent. It is also clear, however, that in man the administration of halothane may be accompanied by bradycardia and hypotension (Johnstone, 1956; Abajain et al., 1958) and studies on the canine heart-lung preparation (Burn et al., 1957) and in the intact dog (Long and Pittinger, 1958) have led to the conclusion that the hypotensive action of halothane is in part due to depression of the myocardium.

It is of interest to ascertain whether the hypotensive action of halothane is due to changes in peripheral resistance such as might result from ganglionic blockade or to a reduction of cardiac output. In addition, it is important to establish the extent of the cardiovascular changes and correlate them accurately with anaesthetic depth. The studies described below were designed to supply this information.

METHODS

Observations were made on 28 normal children who were about to undergo elective surgical procedures. Cardiac output was estimated from dye curves after the method of Hamilton et al. (1928). The concentrations of dye were recorded by an automatic computing ear oximeter developed in this laboratory (Sekelj et al., 1951, 1958a) following the peripheral injection of Evan's Blue. The validity of this technique has been studied and reported elsewhere (Sekelj et al., 1958b). Because of the undesirability of producing blue discoloration of the skin of even a temporary nature, the number of injections had to be limited in any one subject. Instead, therefore, of following continuously the changes due to increasing depths of anaesthesia, maintenance of an anaesthetic level over a period of time and the influence of atropine on these changes in each subject, the study had to be divided into two series.

In the first series (12 subjects), observations were made before and during the administration of 1 per cent halothane and in 7 of these, observations were continued following the administration of atropine. In the second series (16 subjects), the influence of moderate and deep surgical anaesthesia was studied and in 7 of these subjects the same level of anaesthesia was maintained for some time to assess the influence of the duration of the anaesthetic. In 22 studies continuous recordings were obtained of the electrocardiogram (lead 2) and in all except 4 cases the systolic, diastolic and electrically integrated mean blood pressure was recorded via a brachial arterial needle, a strain gauge manometer (Statham P-23D) and a four-channel polygraph (Sanborn). In 4 subjects blood pressure was recorded with a sphygmomanometer at minute intervals and the mean pressure estimated as the sum of the diastolic pressure plus two-thirds of the pulse pressure. Finally, intermittent observations of arterial saturation were made by the same ear oximeter in all cases. In neither series was this observed to fall below 94 per cent.

SERIES 1

In the first series of 12 subjects no premedication was given. Anaesthesia was commenced through a nonrebreathing circuit with 80 per cent nitrous oxide in oxygen which was changed to 50 per cent nitrous oxide in oxygen after induction. A

* Medical Associate of the National Research Council of Canada.

control dye injection was then made, and as soon as it was complete 1 per cent halothane was given in addition by a previously calibrated Rowbotham bottle. After an interval of from 4 to 19 minutes, when heart rate and blood pressure had become stabilized, a second dye injection was made. In 7 subjects the anaesthesia was maintained and atropine sulphate, 0.2 mg, was given by intravenous injection. When this had clearly taken effect, as judged by the heart rate, a third dye injection was made.

Results.

"Basal" values for cardiac output are always difficult to obtain and particularly so in children, but it is probable that nitrous oxide of this percentage has a negligible influence on the cardiovascular system (Prime and Gray, 1952). The values obtained (table I) are comparable to those reported in the literature (Stead et al., 1948; Cournand et al., 1945; Nicholson and Wood, 1951). The changes following the addition of 1 per cent halothane are recorded in table I and figure 1. There was a reduction of cardiac output (mean 16.4 per cent) which was greatest in those with the highest control values. This fall was chiefly the result of a slowing of heart rate and, possibly, to a lesser extent, to a reduction in stroke volume. This latter change was, however, not statistically significant. There was a small fall of mean blood pressure in most cases (mean 14.7 per cent) without significant alteration in the calculated peripheral resistance. Atropine-induced tachycardia resulted in a restoration of cardiac output and blood pressure without significant alteration of stroke volume or peripheral resistance.

It was tentatively concluded from this study that the fall in blood pressure, following the administration of 1 per cent halothane, was the result of a reduction of cardiac output and was not due to a reduction in peripheral resistance; that the changes were small and comparable to those that might be anticipated from changing from very light to moderately deep drug-induced sedation.

Series 2

In this series (16 subjects) an additional recording was made of the electroencephalogram, the electrodes being placed on the frontal region and on one ear lobe (Grass Polygraph). Premedication was given, consisting of oral pentobarbitone (1.7 mg per kg) 2 hours, and morphine (0.12 mg per kg) and scopolamine (0.01 mg per kg) subcutaneously, 1 hour before the study. Induction was completed with nitrous oxide 50 per cent in oxygen and 0.25 per cent halothane via a Fluotec* apparatus using a system with no rebreathing. The nitrous oxide-oxygen mixture was continued throughout the study. Patients were then intubated under the temporary influence of suxamethonium chloride and as soon as they appeared stable the first dye injection was made. The dose of halothane was then increased using the electroencephalogram as a guide until records were obtained corresponding to pattern B or C in figure 2. This required a dose of halothane varying from 2 to 3 per cent in different subjects and corresponded to a depth of anaesthesia clinically estimated at plane 2 or 3. When stable, a second dye

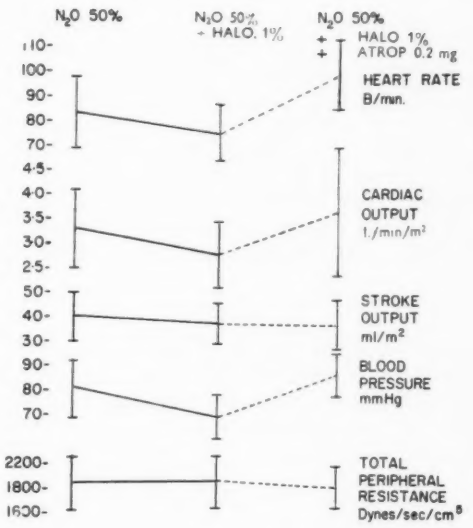

FIG. 1

The cardiovascular effects of 1 per cent halothane and the changes observed following the intravenous injection of 0.2 mg atropine sulphate. Mean values and one standard deviation (vertical bars) are shown. Fifty per cent nitrous oxide in oxygen maintained throughout.

* Cyprane, Ltd., Haworth, Keighley, Yorkshire, England.

TABLE I (SERIES 1)

Comparison of the cardiovascular effects of 1 per cent halothane (injection No. 2) with the control values under 50 per cent nitrous oxide alone (injection No. 1) and the effect of an injection of atropine sulphate, 0.2 mg i.v. (injection No. 3). Below are recorded the mean values, standard deviations (S.D.), and standard deviation of the differences (s.d.d.) between the means of the observations recorded at each injection.

Subject	Age, years	Sex.	Wt. Kg	B.S.A. M^2	Halothane %	Injection No.	Interval min.	Mean B.P. mm Hg	H.R. B/min	Cardiac output l/min/m^2	Stroke output ml/m^2	T.P.R. dynes/sec cm^5
1	11	M	36.6	1.17	0	1	0	83	60	2.28	39	2480
					1	2	5.5	65	55	2.13	39	2083
					1	3	2.5	95	90	3.60	41	1808
2	13	F	41.9	1.32	0	1	0	68	63	4.26	67	1130
					1	2	7	61	60	3.05	51	1201
3	10	M	30.9	1.18	0	1	0	70	73	2.83	39	1676
					1	2	9	67	75	2.66	36	1696
					1	3	4.5	73	90	3.03	34	1634
4	11	F	25.1	0.95	0	1	0	107	84	4.02	48	2295
					1	2	10	73	72	2.88	40	2128
					1	3	1.5	90	96	4.07	42	1814
5	10.5	F	25.0	0.96	0	1	0	90	84	3.06	36	2432
					1	2	6.5	75	78	2.75	35	2266
					1	3	2.5	94	120	3.54	30	2200
6	11	M	30.3	1.07	0	1	0	73	90	2.80	31	1950
					1	2	4	73	80	2.15	27	2547
					1	3	2	83	100	2.93	29	2119
7	10	F	35.6	1.22	0	1	0	74	100	3.96	40	1220
					1	2	5	63	72	3.38	47	1220
8	5	M	17.6	0.73	0	1	0	70	102	3.75	37	2035
					1	2	10	54	90	3.35	42	1715
9	13	F	41.5	1.35	0	1	0	84	81	2.66	33	1822
					1	2	7	76	66	2.09	32	2176
10	9	F	26.2	1.01	0	1	0	95	108	3.81	35	2018
					1	2	7	83	90	2.99	33	2241
11	12	M	40.9	1.36	0	1	0	80	78	1.95	25	2421
					1	2	19	61	78	1.72	22	2085
					1	3	4	78	84	2.20	27	2073
12	10	F	20.0	0.85	0	1	0	80	84	4.25	51	1773
					1	2	12	79	87	3.95	45	1596
					1	3	1.5	90	116	6.22	54	1161
Mean			30.97	1.098	0	1		81	84	3.30	40	1938
					1	2		69	75	2.76	37	1913
					1	3		86	99	3.66	37	1830
S.D.						1		12	15	0.80	11	446
						2		9	11	0.65	8	425
						3		8	14	1.28	10	357
s.d.d.						1–2		9	9	0.36	6	300
p<								0.001	0.01	0.001	0.20	0.0
s.d.d.						2–3		8	12	0.67	5	179
p<								0.01	0.01	0.01	0.40	0.0

injection was made. In 4 subjects the level of anaesthesia was deepened further to correspond with electroencephalographic pattern C or D and deep clinical plane 3, and a third dye curve was obtained. In 7 others an attempt was made to maintain the same level of anaesthesia as judged by the electroencephalographic pattern for periods of time varying from 10 to 26 minutes (mean 16 minutes) before making the final dye injection.

Results.

The results of this series are listed in table II and table III. The control values are closely comparable to those obtained in the first series under

50 per cent nitrous oxide alone (see figure 3) and from this it was concluded that the cardiovascular effects exerted by the premedication and 0.25 per cent halothane were negligible.

The electroencephalographic patterns associated with halothane have been described and found to correlate roughly with the depth of anaesthesia (Robson and Sheridan, 1957; Gain and Paletz, 1957). We were able to confirm this. For descriptive purposes we have arbitrarily classified the electroencephalogram into 4 patterns which have been designated A, B, C, and D (fig. 2).

With increasing concentrations of halothane there was progressive depression of the cardiac output whether this was correlated with the electroencephalographic pattern or with clinical assessment of surgical plane (figs. 4 and 5). The mean reduction of cardiac output at plane 2 was 15 per cent and at plane 3, 23 per cent (fig. 3). Blood pressure fell more or less proportionately with cardiac output and there was a small, though statistically insignificant, elevation of vascular resistance at plane 2. Maintenance of a constant anaesthetic level over an average period of 16 minutes resulted in no further reduction of cardiac output or blood pressure and there was, in fact, some elevation of these values with time (table III and fig. 6).

DISCUSSION

Although not directly relevant to the problem of myocardial depression, it is worth recording that in the 22 instances in which electrocardiograms were recorded there were temporary nodal and ventricular extrasystoles while under 1 per cent

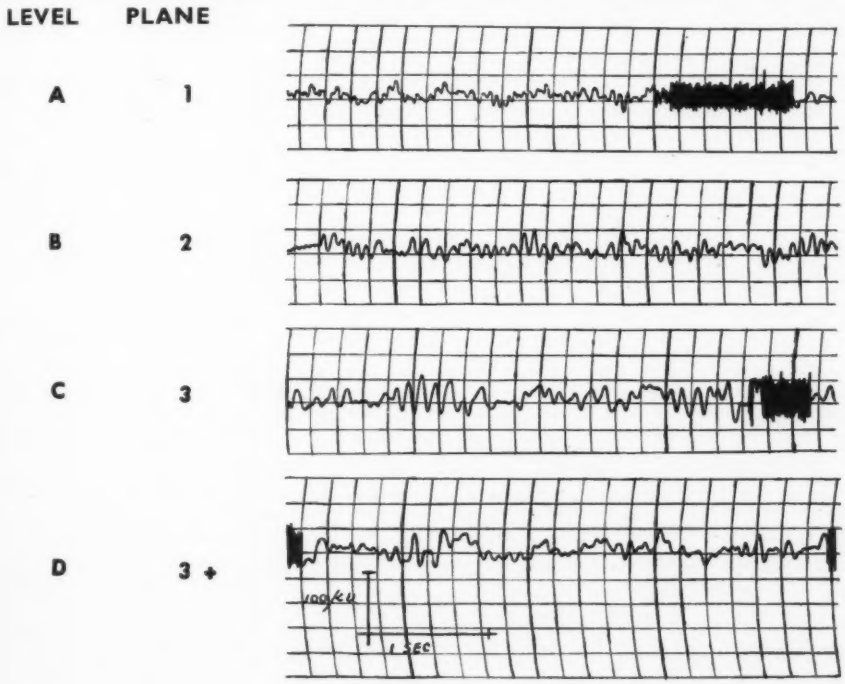

FIG. 2

Representative electroencephalographic tracings obtained under varying levels of halothane anaesthesia (case No. 4, II). These patterns have been arbitrarily designated A, B, C, D.

TABLE II (SERIES 2)

Comparison of cardiovascular effects of three degrees of halothane anaesthesia. Below are recorded the mean values at each plane, the standard deviations (s.d.) and the standard deviation of the differences (s.d.d.)

Subject	Age, years	Sex.	Wt. Kg	B.S.A. M^2	Halothane %	Plane	E.e.g.	Interval min.	Mean B.P. mm Hg	H.R. B/min	Cardiac output l/min/m^2	Stroke output ml/m^2	T.P.R. dynes/sec/cm^5
1	9	M	29.3	1.04	0.25	1	A		85	78	3.19	40.9	2048
					2.0	2	C	10	72	78	3.01	38.6	1840
2	12	M	34.1	1.19	0.5	1	B		87	90	2.30	25.6	2534
					2.0	2	C+	11	79	86	2.12	24.6	2509
					3.0	3	C+	6	80	90	2.40	26.9	2218
3	9	M	27.1	0.97	0.25	1	A		80	84	4.47	53.3	1472
					2.0	1	B	5	81	84	3.44	40.9	1932
4	8	M	22.4	0.89	0.25	1	A		77	66	2.69	40.9	2562
					2.0	2	C	5	67	60	2.24	37.5	2688
					3.0	3	D	2	67	60	1.75	29.8	3433
5	6.5	M	21.8	0.86	0.25	1	B		79	96	2.83	29.5	2598
					2.0	2	B	5	72	96	2.64	27.4	2541
					3.0	3	D	4	71	96	2.41	25.1	2738
6	10	M	31.6	1.09	0.25	1	B		94	90	3.21	35.7	2146
					2.0	2	C	5	85	84	2.77	33.0	2248
					3.0	3	C	5	79	84	2.58	30.7	2245
7	11	F	32.1	1.13	0.25	1	A		88	108	3.63	33.6	1720
					3.0	3	C	16	78	96	1.92	19.9	2870
8	7	M	22.7	0.87	0.25	1	B		84	90	2.55	28.3	3011
					1.75	2	C+	6	77	96	2.22	23.1	3172
9	7	M	15.6	0.69	0.25	1	A		70	72	3.01	41.8	2685
					2.0	3	C	6	65	66	2.29	34.6	2460
10	5	M	18.4	0.72	0.25	1	A		77	90	3.31	36.8	2582
					2.0	2	C+	5	68	96	2.43	23.2	3268
11	6.5	F	14.4	0.67	0.25	1	A+		78	100	4.51	45.1	2061
					2.5	2	C	6	69	106	3.73	35.2	2208
12	10	M	33.3	1.13	0.25	1	A		83	84	1.92	22.9	3058
					2.5	2	C	7	76	78	2.06	26.4	2618
13	9	M	26.9	1.05	0.25	1	A		85	78	3.67	45.0	1712
					2.25	3	C+	15	72	80	3.07	36.6	1783
14	9	M	34.4	1.11	0.25	1	A		80	81	2.53	31.2	2277
					2.5	3	C	12	70	75	2.56	34.0	1975
15	13	M	30.4	1.13	0.25	1	A		80	84	2.43	28.9	2367
					2.5	3	D	9	69	78	2.33	29.8	2099
16	5.5	M	20.1	0.79	0.25	1	A		75	90	3.90	43.4	1945
					2.0	3	C	4	69	90	2.92	32.4	2394
Mean			25.9	0.96		1			81	86	3.13	36.4	2302
						2			75	86	2.67	31.0	2502
						3			72	82	2.42	30.0	2422
s.d.						1			6	10	0.75	8.4	455
						2			6	13	0.57	6.8	471
						3			5	12	0.41	5.0	484
s.d.d.						1–2			4	5	0.37	5.4	317
p<									0.001	0.90	0.01	0.02	0.40
s.d.d.						1–3			3	4	0.54	5.8	513
p<									0.001	0.02	0.01	0.2	0.40

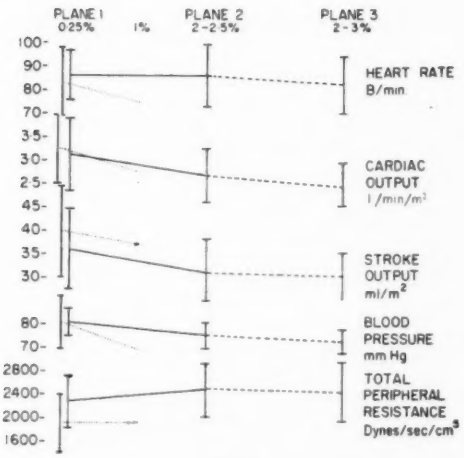

FIG. 3

Comparison of cardiovascular effects of halothane at varying levels of anaesthesia. Mean values and one standard deviation (vertical bars) are shown. The control values and values on 1 per cent halothane observed in series I are represented by the fine dotted lines for comparison.

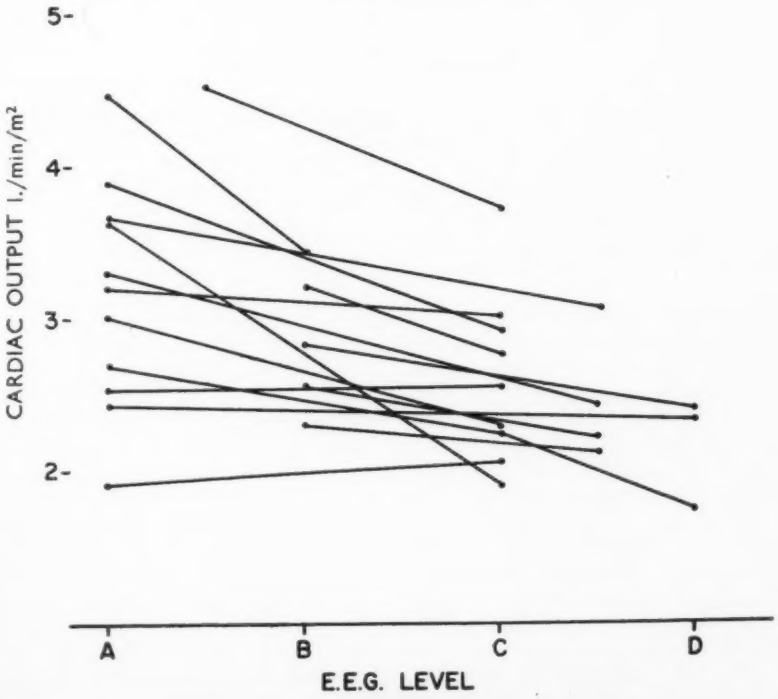

FIG. 4

The relationship between cardiac output and varying levels of anaesthesia as determined by the electroencephalogram.

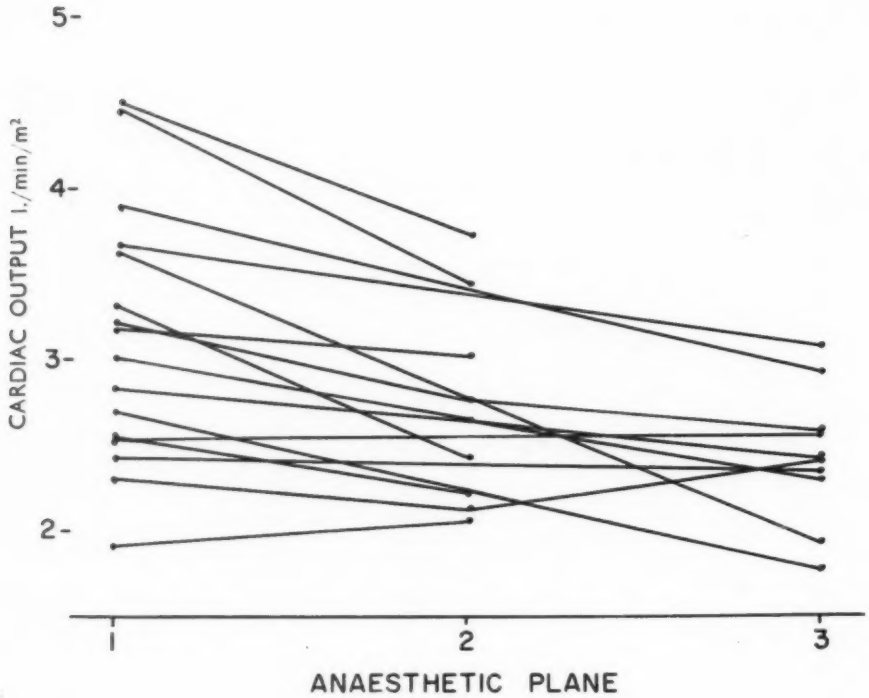

FIG. 5

The relationship between cardiac output and anaesthetic plane determined on clinical criteria (Guedel, 1937).

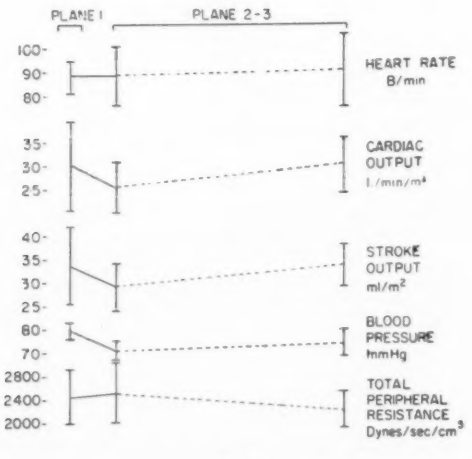

FIG. 6

The cardiovascular effects of maintaining as constant a level as possible of moderately deep halothane anaesthesia over an average period of 16 minutes (10 to 26 minutes). The mean values and standard deviation (vertical bars) obtained in 7 subjects are shown.

TABLE III (SERIES 2)

The cardiovascular effects of inducing a moderately deep level of halothane anaesthesia and maintaining it as constantly as possible. It will be noted that to maintain a constant e.e.g. and clinical level it was frequently necessary to alter the concentration of halothane.

Subject	Age, years	Sex.	Wt. Kg	B.S.A. M^2	Halothane %	Plane	E.e.g.	Interval min.	Mean blood pressure	H.R. B/min	Cardiac output l/min/m^2	Stroke output ml/m^2	T.P.R. dynes/sec/cm^5
8	7	M	22.7	0.87	0.25	1	B		84	90	2.55	28.3	3011
					1.75	2	C+	6	77	96	2.22	23.1	3172
					2.0	2	C	10	79	96	2.72	28.3	2659
10	5	M	18.4	0.72	0.25	1	A		77	90	3.31	36.8	2582
					2.0	2	C+	5	68	96	2.43	23.2	3268
					2.5	2	D	15	67	102	3.08	30.1	2420
11	6.5	F	14.4	0.67	0.25	1	A		78	100	4.51	45.1	2061
					2.5	2	C	6	69	106	3.73	35.2	2208
					2.0	2	C	20	68	110	4.31	30.1	1880
12	10	M	33.3	1.13	0.25	1	A		83	84	1.92	23.0	3061
					2.5	2	C	7	76	78	2.06	26.4	2618
					2.0	2	C	26	80	78	2.70	34.6	2099
14	9	M	34.4	1.11	0.25	1	A		80	81	2.53	31.2	2277
					2.5	3	C	12	70	75	2.56	34.0	1975
					2.2	3	C	14	75	75	2.98	39.7	1814
15	13	M	30.4	1.13	0.25	1	A		80	84	2.43	28.9	2367
					2.5	3	D	9	69	78	2.33	29.8	2099
					2.5	3	D	16	74	72	2.39	33.2	2193
16	5.5	M	20.1	0.79	0.25	1	A		75	90	3.90	43.4	1945
					2.0	3	C	4	69	90	2.92	32.4	2394
					1.5	3	B	13	75	102	3.19	31.3	2380
Mean			24.8	0.92	Control observation				80	88	3.02	33.8	2472
					Plane 2, 3 (initial)				71	88	2.61	29.2	2533
					Plane 2, 3 (final)				74	91	3.05	33.8	2206
s.d.					Control deviations				3	6	0.92	8.2	437
					Plane 2, 3 (initial)				4	12	0.57	5.0	513
					Plane 2, 3 (final)				5	15	0.62	4.4	304
s.d.d.					Initial and final				3	6	0.22	3.0	328
$p<$									0.05	0.40	0.01	0.01	0.05

halothane in Case No. 1, and a temporary nodal rhythm while receiving 2 per cent halothane in Case No. 23. Normal rhythm returned spontaneously in each case.

Halothane anaesthesia has been employed with 50 per cent nitrous oxide and oxygen in this hospital using the premedication outlined above on 4,074 occasions without fatality or any serious complication related to the anaesthetic agent. The use of any drug to raise the blood pressure has not been necessary. Induction is made with 1½ to 2 per cent halothane which is then reduced to ½ per cent for maintenance of anaesthesia. It has not been employed in situations where profound relaxation is required and has rarely been used with assisted ventilation. Employed in this manner it has proved an extremely useful anaesthetic agent, its advantages having already been set forth by several workers (Brennan, Hunter and Johnstone, 1957; Bryce-Smith and O'Brien, 1957; Abajain et al., 1958; Pope, 1957). These advantages, coupled with its noninflammable nature, make strong reasons for its retention as an anaesthetic agent unless good evidence of toxicity is produced. The influence of this drug on the myocardium is, thus, of considerable clinical importance.

Although undoubted depression of cardiac function by halothane has been demonstrated in the dog heart-lung preparation (Burn et al., 1957) and in the intact dog (Long and Pittinger, 1958; Krantz et al., 1958), this is an action shared, as these authors have shown, by ether, cyclopropane,

and chloroform. Evidence that halothane in anaesthetic doses in man is a significant myocardial depressant is, however, less certain. The principal evidence on this point has resulted from the work of Severinghaus and Cullen (1958). These authors demonstrated, firstly, reductions of cardiac output out of proportion to the observed fall of oxygen uptake and, secondly, they pointed to the fall in cardiac output which occurred with halothane in the presence of an elevation of venous pressure. They pointed to these as two strong indications of depression of myocardial function.

Simple evidence of a reduction of cardiac output under anaesthesia does not necessarily imply myocardial depression. Oxygen uptake is also reduced under anaesthesia and in the case of 1.5 per cent halothane this has been shown by Severinghaus and Cullen to amount to a 15 to 20 per cent reduction in oxygen requirements. A fall of cardiac output in proportion to this might be interpreted as a normal response. The reduction in cardiac output, resulting from concentrations of 2 to 2.5 per cent of halothane, in our study, produced a mean reduction of cardiac output of only 15 per cent and, although oxygen uptake was not measured by us, comparison of these values with the 15 to 20 per cent reduction in oxygen uptake observed by Severinghaus and Cullen suggests the depression of cardiac output was not out of proportion to the probable reduction in metabolic rate. The greater reduction of cardiac output (31 per cent) observed by these authors with an anaesthetic concentration of 1.5 per cent halothane, is most likely the result of the positive pressure ventilation which they employed. As they observed, it is likely that the elevation of intrathoracic pressure resulting from this would be sufficient in an anaesthetized patient to diminish venous return and cardiac output significantly. Hypoxia was not a factor in our cases, but it is not unlikely that the higher cardiac output values obtained in our study at deeper levels of anaesthesia were partly a result of the inevitable hypoventilation and carbon dioxide retention which accompanies deeper levels of halothane anaesthesia (Long and Pittinger, 1958; Devine et al., 1958).

The fact that cardiac output fell in the presence of elevated central venous pressure in the experiments of Severinghaus and Cullen might also be the result of positive pressure ventilation. In the absence of a change of intrathoracic pressure, this elevation of venous pressure with reduced cardiac output would represent strong evidence of myocardial depression. But the degree of positive pressure used by them is not inconsistent with the elevation of venous pressure they observed and might not, in fact, represent a true elevation of ventricular distending pressure at all.

At present it can be tentatively concluded that the fall of blood pressure observed in man with anaesthetic doses of halothane is primarily the result of depression of cardiac output, but there seems as yet to be insufficient evidence to conclude that this represents myocardial depression. It is then, pertinent to enquire why the blood pressure is depressed to a greater extent with halothane than with other anaesthetics. Is this due to a greater reduction of cardiac output or to a difference in vasomotor tone? Comparison of halothane with the reported actions of other anaesthetic substances is not easy as there is great variability of such factors as age, premedication, anaesthetic depth and concurrent surgical intervention, but some evidence is available for consideration.

Cyclopropane, while depressing cardiac output in the dog heart-lung preparation (Prime and Gray, 1952) is, apparently, associated with an increase of output in the intact dog (Gersheimer et al., 1954; Robbins and Baxter, 1938). In a study of 7 adult human subjects, however, Thompson, Patrick and Wood (1957) demonstrated reductions in cardiac output of 29 per cent and 40 per cent with light and deeper levels of cyclopropane anaesthesia respectively. These are considerably greater reductions than were observed in our study, but it should be noted that these workers, too, used artificial ventilation. They concluded that a depression of cardiac output in association with an elevation of central venous pressure was the result of direct depression of the myocardium by cyclopropane. The most striking difference between cyclopropane and halothane, however, would appear to lie in the reaction of the peripheral vasculature. Halothane administration resulted in a small (not statistically significant) elevation of peripheral resistance in our study and also in the investigation reported by Severinghaus and Cullen and there was, con-

sequently, a fall in the arterial pressure which more or less paralleled the fall in cardiac output. With cyclopropane, by contrast, there appears to be a striking elevation of vascular resistance and arterial pressure with progressively deeper levels of anaesthesia.

Thiopentone has been shown to depress cardiac action in the dog heart-lung preparation (Prime and Gray, 1952) though it, too, produces an increase of output in the intact dog (Gersheimer et al., 1953). Two studies in man have both demonstrated considerable reductions of cardiac output at levels of surgical anaesthesia (Li et al., 1954; Ridley and Wood, 1955). Blood pressure becomes slightly reduced, though this is not marked, due to an elevation of vascular resistance which partly compensates for the lower output.

Ether on the dog heart-lung preparation has been repeatedly demonstrated to depress myocardial function (Prime and Gray, 1952; Brewster, 1953) though with an intact sympatho-adrenal system this effect may be small (Burn et al., 1957). In the intact dog ether has been associated with an increase of output (Gersheimer et al., 1954b) while in man, though the response is variable, there is probably a consistent reduction of output in the absence of a period of excitement during the stage of induction (Fletcher, Pender and Wood, 1956). These authors observed no systematic effect on blood pressure.

Thus, while there is evidence that cyclopropane, thiopentone, ether as well as halothane and chloroform depress myocardial function in the heart-lung preparation, this does not allow a prediction of their influence in man under clinical conditions. Their effect in man will vary with, amongst other factors, the extent and manner in which they elicit or depress the responses of the autonomic nervous system. In judging halothane as an anaesthetic agent it is possible to conclude that it shares with other agents a tendency to reduce the cardiac output; that, at least when used by the technique outlined above, this depression of output does not seem to be greater than other agents on which information exists; and that there is not yet sufficient evidence to indicate that this reduction of output is related to myocardial depression. The observed reductions in blood pressure occurring when halothane is used in this manner have not been marked and are the result of an inadequate or absent increase of peripheral resistance to compensate for the reduced output. From the point of view of an anaesthetic agent, this might be considered an advantageous phenomenon.

SUMMARY

The cardiovascular effects of varying depths of halothane anaesthesia were observed in 28 normal children.

It was shown that 0.25 per cent halothane and 50 per cent nitrous oxide in oxygen preceded by medication with pentobarbitone, morphine and scopolamine had no significant effect on heart rate, cardiac output and blood pressure, using the values obtained under 50 per cent nitrous oxide alone as control.

Moderate and deep levels of halothane obtained by using concentrations of 2 to 3 per cent with spontaneous respiration produced reductions of cardiac output of the order of 15 and 23 per cent, respectively.

There was a failure of vascular resistance to rise proportionately to the reduction of output observed, with a resultant moderate fall of blood pressure. There is evidence from the literature that these values were almost certainly influenced by a degree of hypoventilation and carbon dioxide retention.

Comparison of these results with the evidence available from the literature does not suggest that the reductions of cardiac output and arterial pressure observed with halothane are greater than those occurring with other anaesthetic agents, nor does there seem to be, as yet, sufficient evidence to attribute these changes to myocardial depression.

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S.C.T.Z.—A NEW INTRAVENOUS ANAESTHETIC?

BY

JOHN W. DUNDEE

*Department of Anaesthesia, Queen's University of Belfast, Belfast, Northern Ireland**

As a result of an investigation into the shock produced by the intravenous injection of thiamine chlorhydrate (vitamin B_1), Charonnat, Lechat and Chareton (1953a, b, c) identified two distinct structures in the thiamine nucleus (fig. 1). Experiments showed that only the pyrimidine part was responsible for producing shock and that its stimulating action was opposed by the strongly depressant thiazole fraction. A number of derivatives of the thiazole fraction were then prepared and the hypnotic and sedative properties of one of these products (S.C.T.Z.) were confirmed clinically by Charonnat, Lechat and Chareton (1957). These workers also carried out chronic toxicity tests with S.C.T.Z. and demonstrated its anticonvulsant action in animals. The drug was shown to have no deleterious effects on the respiration or cardiovascular system of the rabbit, to be devoid of antihistamine activity and to have no curarizing action.

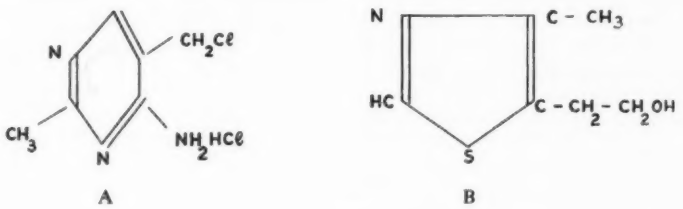

FIG. 1

Two distinct fractions in the formula of Vitamin B_1.

A. The pyrimidine type
The chlorhydrate of methyl-2-amino-4-chloromethyl-5-pyrimidine

B. The thiazole type
Methyl-4-β-hydroxyethyl-5-thiazole

A clinical study of the use of S.C.T.Z. in anaesthesia was carried out by Laborit and his colleagues, who reported the results obtained in 80 cases in 1957. Their main finding was that the drug could rapidly produce sleep, yet the patient would continue to react to stimuli, no matter how deeply anaesthetized. No potentiating action with the volatile, gaseous or intravenous anaesthetics was observed. Neuromuscular transmission was unaffected by S.C.T.Z., and reflex activity was either unchanged or slightly enhanced with a slight increase in muscle tone. A variable degree of tachycardia and hypotension followed the intravenous injection of a dose sufficient to produce sleep, and severe tachycardia occurred after endotracheal intubation or other stimulation. Oxygen consumption was unaltered by S.C.T.Z. No disturbances in electrolytes were noted and nausea and vomiting after operation did not occur. There were no adverse local effects following injection.

The nearest approach to good surgical anaesthesia achieved by these French workers was with an induction by S.C.T.Z. followed by promethazine and pethidine and a continuous infusion of a

* This work was done at the Department of Anaesthesia, University of Liverpool.

dilute solution of S.C.T.Z. In some cases chlorpromazine and hydergine were also used. Because of the multiplicity of drugs employed, it was very difficult to draw any definite conclusions from this publication as to the value of S.C.T.Z. in anaesthesia.

Attention has also been drawn to this preparation in an annotation in the *British Medical Journal* in 1957. This suggested that S.C.T.Z. may prove "a useful tool for the doctor".

This paper reports a clinical trial of the drug in 40 cases. Where possible its action was compared with that of thiopentone which is the drug most frequently used in intravenous anaesthesia.

PHYSICAL PROPERTIES

The thiazole part of thiamine in a pure form is a colourless liquid; its hydrochloric ester is also a liquid, but the salts form white solids with a characteristic smell and taste. They are nearly all unstable in air.

The chemical composition of S.C.T.Z. is shown in figure 2. (It is not possible to say how the letters S.C.T.Z. were derived from the formula shown.) S.C.T.Z. is a colourless powder or crystals with a characteristic odour and melting point of 124°C. It is soluble in water, ethanol and methanol and insoluble in ether and benzene. The injectable preparation used was identical with that of the French workers and the 2 per cent solution was prepared as follows:

S.C.T.Z	2 g
Glucose	2 g
NaOH	2 ml
Distilled water to	100 ml

SELECTION OF CASES

S.C.T.Z was used only in fit adult patients undergoing a variety of general or neurosurgical procedures. Availability of time for the induction of anaesthesia and of help in recording data were the only factors in deciding whether a fit patient received S.C.T.Z. or thiopentone for the induction of anaesthesia. Within the limitations stated, and except for a brief period where a 1 per cent solution of thiopentone was used for comparison, S.C.T.Z. was employed almost routinely by the author for approximately three months.

ANAESTHETIC TECHNIQUES

Initially it was planned first to use S.C.T.Z. as sole narcotic for minor procedures such as incision of abscesses, dressing of burns and examinations under anaesthesia. This was attempted in five patients, but for reasons which will be obvious later this technique was unsatisfactory and all five patients also required an intravenous barbiturate to produce surgical anaesthesia. No data is included from this group of cases.

Following this unsatisfactory start, it was decided to employ S.C.T.Z. for more major surgery in a manner similar to thiopentone and to prefer instances where a long-acting muscle relaxant would not be required. The distribution of the use of various techniques is shown in table I. There were two additional cases in which, by virtue of the quality of the anaesthesia, the use of S.C.T.Z. had to be abandoned during the induction and thiopentone used. These patients were in groups 1 and 2 and are not included in the final analysis of the data.

Techniques were standardized as far as possible and all anaesthetics were given personally by the author. Gas flows in nonrelaxant cases consisted of 6 litres of nitrous oxide and 2 litres of oxygen per minute. Only one analgesic was used throughout, consisting of a mixture of pethidine and levallorphan in concentration ratio of 100 to 1.25.

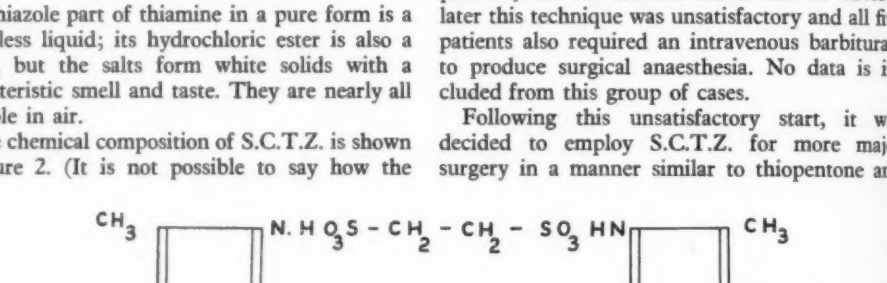

FIG. 2

Chemical structure of S.C.T.Z.
Ethane disulphonate of methyl-4-β-chlorethyl-5-thiazole.

TABLE I

Distribution of various anaesthetic techniques in this study.

Group	Technique	Number of cases
1	S.C.T.Z. as a basal narcotic, followed by N_2O—O_2 and a volatile agent—no relaxant	6
2	S.C.T.Z.—N_2O—O_2 attempted	5
3	As above with long-acting muscle relaxant	6
4	S.C.T.Z.—N_2O—O_2—analgesic	11
5	As above with long-acting muscle relaxant	5
	Total	33

This will be referred to by the proprietary name of Pethilorfan, and in the tables the dosage of pethidine only will be given. This combination was chosen because of reports by Swerdlow (1957) on its minimal depressant action on respiration, thus enabling the effect of the S.C.T.Z. to be observed. In groups 3 and 5 d-tubocurarine chloride was used exclusively as the muscle relaxant, with reversal of its action by atropine and neostigmine at the end of the anaesthesia. When endotracheal intubation was used in the other groups this was carried out with the help of suxamethonium (40–50 mg) and the larynx and trachea sprayed with a 4 per cent solution of lignocaine.

No apology is made for reporting such a small number of cases with a variety of techniques. Subsequent data will show that, in fact, it would not have been justified to extend this investigation unless all patients required a long-acting muscle relaxant. It was felt that data from such cases would be of little value as far as information on the action of the narcotic itself was concerned.

METHOD OF ASSESSING RESULTS

There was a great individual variation among the patients, both in regard to their requirements of the drug and in the quality of the anaesthesia produced by narcotic doses. The latter varied from a smooth induction and maintenance to conditions which made surgery extremely difficult. To simplify the analysis of data, all administrations have been reviewed and the results classified as follows:

Grade 1. Smooth induction and maintenance—similar to expectations from an intravenous thiobarbiturate.

Grade 2. Troublesome coughing, hiccough, uneven anaesthesia, movement by patient, etc. Operating conditions fair.

Grade 3. Very troublesome with extremely poor operating conditions.

In tables II–IV the induction period has been classified as above from the viewpoint of the anaesthetist, and the maintenance of anaesthesia from the viewpoint of the surgeon. It should be mentioned that the above classification only deals with the actual conditions produced by the drug for the circumstances stated and does not make allowances for its effect on the cardiovascular and respiratory systems. While data on these latter actions is available, this will not be described in the same detail. It is felt that the prime requirement of an intravenous narcotic is to produce sleep and good operating conditions with the same ease as is experienced with the recognized drugs. Only when these criteria are fulfilled is it necessary to analyze critically the side effects and compare these with those of other drugs.

The exact time taken from the end of the operation to recovery of protective reflexes and return to consciousness (as judged by ability to answer questions) was not recorded in every case. Where this exact data is not available the times are recorded as rapid, slow and very slow. These are simply a comparison of the recovery time with what would be expected from the use of thiopentone under similar conditions.

CLINICAL DATA

As mentioned previously, only the cases in which a long-acting relaxant was not used are described in detail. Details of cases in these groups are given in tables II and IV.

Induction of anaesthesia.

One of the obvious drawbacks of S.C.T.Z is that it is necessary to use a 2 per cent solution. The drug does not approach thiopentone in potency and thus large volumes of solution have to be used. After 20 ml the average patient felt sleepy within 30–40 seconds and the rapid injection of a second similar dose would usually cause the patient to yawn and the corneal reflex may

TABLE II

Data of 6 cases in which S.C.T.Z. was used as a basal narcotic.

No.	Sex	Age	Operation	Duration (min)	Pre-op. med.	S.C.T.Z. Ind. (g)	S.C.T.Z. Supp. (g)	S.C.T.Z. Total (ml)	Induction Grade	Induction Time (min)	Anaesthesia grade	Supplementary agents E	Supplementary agents TCE	Supplementary agents Analg.	Recovery Reflexes	Recovery Final	Comment
1	M	39	Laminectomy	135	A	0.8	0.8	80	1	25	1	+	+		Rapid	Rapid	
2	M	46	Laminectomy	240	A	1.6		80	2	30	2		+	P 25	Rapid	Slow	Hiccough*
3	F	53	Vein stripping	60	P	1.2	1.7	145	3	15	2		+	P 80	60 min	2–3 hr	Coughing†
4	M	32	Bouginage	17		0.6		30	1	5	1	+		P 20	3½ hr	Slow	Venous thrombosis
5	F	68	Mastectomy	155	P	0.5		25	1	25	1		+		15 min	3 hr	
6	F	53	Mastectomy	145	P	0.8	0.4	60	3	45	2		+	P 50	Slow	Very slow	Coughing†

All patients received atropine 0.6 mg in addition to pre-operative medication shown and all were maintained with N_2O—O_2. Intubation was carried out with the help of suxamethonium.

Key: For grades of induction and anaesthesia see text.

Pre-operative medication: A=Analgesic drug; P=Promethazine.
Supplementary agents: E=Ether; TCE=Trichloroethylene; P=Pethilorfan (mg).

Comment: *Could not carry on with N_2O—O_2—TCE because of tachypnoea: Pethidine (20 mg) given to slow rate.
† Coughing very troublesome during induction. Almost had to abandon use of S.C.T.Z.

TABLE III

Details of 5 cases in which anaesthesia was attempted with S.C.T.Z.—N_2O—O_2 alone.

No.	Sex	Age	Operation	Duration (min)	Pre-op. med.	S.C.T.Z. Ind. (g)	S.C.T.Z. Supp. (g)	S.C.T.Z. Total (ml)	Induction Grade	Induction Time (min)	Anaesthesia grade	Recovery Reflexes	Recovery Final	Comment
1	M	31	Craniotomy	180		1.05	0.95	100	1	20	1	Rapid	Slow	
2	M	30	Haemorrhoidectomy	35	P	1.2	1.8	150	3	25	3	Rapid	1 hr	Pethidine 20 mg and thiopentone 100 mg given*
3	M	36	Vein stripping	130	P	1.6	2.6	210	3	25	3	Rapid	Slow	Thrombosis‡
4	F	53	Mastectomy	110	P	1.2	1.4	130	3	45	2	15 min	1hr	Coughing intermittent
5	M	62	Laminectomy	125	A	0.8	1.8	130	2	20	2	1 hr	4 hr	Never really settled

Abbreviations as in Table II.

Comment: *Thiopentone had to be given in a hurry as control of anaesthesia was lost.
‡ See detailed cases.

disappear. If a further dose is not given immediately this reflex will promptly return and the patient will object to the application of a face mask. Muscular movement in response to any, even minor, stimulus will be marked at this stage if a further needle prick is needed; it may then be necessary to restrain the patient.

One of the great difficulties experienced with S.C.T.Z. was to be certain of when the patient was asleep let alone judge the exact moment when a face mask should be applied or intubation attempted. There were on several occasions repeated attempts by patients made apnoeic with suxamethonium to resist intubation by moving the limbs, and even by trying to remove the tube. Despite this, when each patient was questioned closely at a later date as to their impressions of the onset of anaesthesia, none had any recollections either of the application of the mask or of intubation; all related that they had fallen asleep quietly, shortly after the needle prick. There is no evidence for delay in the onset of sleep as experienced with hydroxydione, and an impression was formed that the effects occurred as rapidly as with thiopentone.

On the basis of the classification already described, S.C.T.Z. was not as satisfactory a drug as thiopentone to precede maintenance of anaesthesia with a gaseous or volatile agent. In some cases induction was very prolonged and the uptake of the volatile agent was delayed by frequent movement, coughing and breath-holding. On one occasion (case 6, table II) a very prolonged and stormy induction occurred and was eventually terminated only by the use of a relaxant and intubation followed by 20 mg Pethilorfan and pulmonary inflation with nitrous oxide-oxygen-trichloroethylene.

Where a volatile supplement to nitrous oxide was not used (table III) induction was even more prolonged and difficult. Two very troublesome situations arose: in one of these (case 2) the situation was only retrieved by the use of 100 mg thiopentone and in the other (case 4) by suxamethonium. The volume of solution needed to induce anaesthesia (40–80 ml) and the induction time (20–45 min) speak for themselves of the disadvantages of this mode of usage of S.C.T.Z.

It was felt that many of the drawbacks of S.C.T.Z. as an induction agent were due to its lack of analgesic potency. Excessive movement at the least stimulation substantiated this view. In table IV all the cases, with one exception (case 7) received a preliminary dose of Pethilorfan about 5 minutes before injection of the S.C.T.Z. This appreciably eased the difficulties of induction, and muscular movement was much less. However, there still remained the problem of deciding when the patient was asleep and the proper time to apply the face mask or perform intubation. Even including case 4, who was particularly resistant to the drug, the average dose of S.C.T.Z. was much less than that employed in the previous two series of cases.

It should be pointed out that the cases (tables II, III and IV) were not anaesthetized consecutively in the order in which they are presented. If this were so the better results in table IV could be attributed to increasing experience with the use of S.C.T.Z. In practice, the techniques were randomized and so it was found that the smoothness of induction did not appreciably alter with experience in using the drug.

Induction of anaesthesia in groups 3 and 5 (table I) where a long-acting relaxant was used were similar to those in the above groups. Again the induction was easier when a preliminary dose of Pethilorfan had been injected. It was always possible to terminate struggling with a large dose of d-tubocurarine and intubation was always easy. Nevertheless, there were a few patients who resisted this manoeuvre a little by movement of limbs and who attempted to remove the tube.

Tables II–IV make frequent mention of the presence of venous thrombosis at the injection site. In six out of the 33 cases this was preceded by pain during the initial injection (table V). This often delayed the induction as the patient would suddenly move the arm and the needle might become dislodged. No patient had any memory of this pain when questioned later.

Maintenance.

There is little that can be said of this aspect of anaesthesia from cases in table II, save that it was not always as smooth as one would have expected after a thiopentone induction. Coughing which started during the induction persisted periodically but to a lesser degree throughout the whole operation in two cases. Tachypnoea always

Abbreviations as in Table II.
Comment: *Thiopentone had to be given in a hurry as control of anaesthesia was lost.
‡ See detailed cases.

TABLE IV

Data on 11 cases anaesthetized with S.C.T.Z.—N_2O—O_2—Pethilorfan.

No.	Sex	Age	Operation	Duration (min)	Pre-op. med.	S.C.T.Z. Ind. (g)	S.C.T.Z. Supp. (g)	S.C.T.Z. Total (ml)	Analgesic (mg) Initial	Analgesic (mg) Supp	Induction Grade	Induction Time (min)	Anaesthesia grade	Recovery Reflexes	Recovery Final	Comment
1	M	49	Vein stripping	50	P	0.8	0.4	60	50	75	1	10	2	Rapid	3 hr	
2	F	17	Cystoscopy	15		1.0		50	50	20	1	5	1	Rapid	Rapid	
3	M	31	Laminectomy	150	A	0.8	0.8	80	25	25	2	15	1	Rapid	Rapid	
4	M	36	Vein stripping	125	P	2.4	1.6	200	40	145	2	15	2	1 hr	3 hr	Thrombosis
5	M	28	Cystoscopy	20		0.6	0.2	40	60	40	1	5	1	Rapid	Rapid	
6	M	20	Excision of cyst	20	P	0.8	0.8	80	50	70	2	10	2	Rapid	1 hr	
7	F	39	Excision of ganglion	25	P	0.8	0.6	70		60	1	5	1	Rapid	2 hr	Thrombosis
8	F	28	Craniotomy	55	A	0.6	0.6	60	80	20	1	5	1	Slow	2 hr	
9	M	17	Craniotomy	255		0.3		15	20	40	1	10	1	Slow	3 hr	Thrombosis
10	M	52	Excision of bursa	35	P	0.4	0.2	80	100	70	3	20	1	1 hr	2 hr	
11	M	29	Craniotomy	195		0.8	0.2	50	20		1	15	1	1 hr	2 hr	

Abbreviations as in Table II.

TABLE V

Summary of some aspects of anaesthesia and sequelae.

Group	No. of cases	Average rating Induction	Average rating Maintenance	Average Duration (min.)	Average Dose of 2% sol. (ml)	Evidence of vein irritation Pain	Evidence of vein irritation Thrombosis
1	6	1.8	1.5	124	70		1
2	5	2.2	2.1	116	144	1	1
3	6	1.6	2.1	160	129	1	2
4	11	1.5	1.4	86	71	3	3
5	5	1.6	1.4	109	75	1	1
	33	1.8	1.6	115	100	6	8

occurred when trichloroethylene was used, but in only one case (no. 2) was pethidine needed to slow the respiratory rate.

From table III, it is obvious that S.C.T.Z.-nitrous oxide-oxygen is not a satisfactory method for maintenance of anaesthesia. Patients moved frequently at the skin incision and also periodically during the operation. Extremely large doses of narcotic were needed to produce even a very indifferent quality of surgical anaesthesia. The notes, made following the most difficult case (case 3, table III), illustrate the difficulties encountered:

This was a 70 kg robust male to have unilateral excision of varicose veins. Induction was very slow; he complained of pain in the arm following the initial injection of the first 10 ml of solution, and had to be forcibly restrained for supplementary injections. Even after 60 ml (1.2 g), it was difficult to say whether he was asleep or not. A further 20 ml was given quickly and the face mask applied. There followed a long struggle and a high concentration of trichloroethylene was used for five minutes.

A further 40 ml (making a total of 2.5 g) of solution were injected just before the skin incision, but even after this the patient moved slightly. A further four skin incisions were made during this operation, and despite the injection of a further 90 ml S.C.T.Z. the patient moved violently at three of these. On one occasion it was absolutely necessary to use in addition 100 mg of thiopentone.

At the end of the operation the nitrous oxide was discontinued as the final skin suture was being tied and there was marked movement when the dressings were being applied. On return to the ward the patient was phonating and extremely restless. Half an hour later he was still restless and shivering intensely. Two hours after the end of the operation he still did not respond to questions or commands.

A painless hard thrombosis was noted at the site of the initial injection and at that of a subsequent injection, but caused no trouble.

In table IV, the results obtained with S.C.T.Z.-nitrous oxide-oxygen-Pethilorfan were fairly satisfactory and it was felt that these were not much worse than would have been achieved if thiopentone had been used in place of the S.C.T.Z. It must be pointed out that extremely large doses of analgesic were used, and with such large doses, supplementary injections of the barbiturate would probably have been unnecessary. Of interest in the table is case 4, the patient described above undergoing a second operation. Anaesthesia was much smoother at the second operation although the requirements of S.C.T.Z. were still very high, and large doses of analgesic (185 mg Pethilorfan) were given.

The inability to continue anaesthesia smoothly with nitrous oxide-oxygen-Pethilorfan (with or without a relaxant) without the need of supplementary doses of the narcotic, makes one wonder if S.C.T.Z. is a pure narcotic without some excitatory action. In none of the cases where d-tubocurarine chloride was used was it possible to continue anaesthesia without supplementary doses of S.C.T.Z., despite hyperventilation and the use of large gas flows at the beginning to wash out alveolar nitrogen. Clinical experience with thiopentone shows that in similar circumstances anaesthesia could have been continued almost invariably with the gas mixture alone.

Recovery.

While it was common to have a return of the protective pharyngeal and laryngeal reflexes at the end of the operation, complete return of consciousness frequently took two to three hours, irrespective of the duration of the anaesthesia or the agents used to supplement S.C.T.Z. There did seem to be the danger of an apparently conscious patient lapsing back into deep sleep when stimulation was stopped. On the whole, the impression was formed that recovery from S.C.T.Z. was not as prompt as one would have expected from doses of thiopentone which produced the same degree of narcosis.

Postoperative restlessness occurred frequently after operation in patients who did not receive an analgesic drug. This was often accompanied by intense shivering. On only one occasion was this so serious as to cause concern, but the incidence was definitely greater than after thiopentone.

Irritant action on veins.

This has been mentioned in discussing the difficulties of induction of anaesthesia with S.C.T.Z. In all cases a careful search was made for the presence of thrombosis of veins on the day after operation and the 24 per cent incidence of the complication is much higher than figures reported by Hutton and Hall (1957) for thiopentone. There were no permanent ill effects from this complication.

Cardiovascular system.

As might be expected from the uneven anaesthesia which was obtained in most cases, the blood pressure and pulse records obtained are of little

value in determining the effects of S.C.T.Z. on the cardiovascular system.

In most cases where endotracheal intubation was carried out with S.C.T.Z. and a muscle relaxant, it was accompanied by a marked and sometimes fairly prolonged rise in blood pressure and tachycardia. There was no relation between this incidence and the nature of the relaxant used, and a typical chart is shown in figure 3. One could not say whether the topical application of lignocaine to the larynx and trachea reduced this reaction as the local anaesthetic was employed to enable patients to tolerate a tube during light anaesthesia, and not to facilitate intubation. It is unlikely that the lignocaine could have been effective by the time intubation was carried out. Skin incision frequently caused a similar but less marked rise in blood pressure.

While S.C.T.Z. did not seem to have a very marked hypotensive action when given intermittently, in three cases a continuous infusion was used to induce and maintain anaesthesia and in all of these some fall in blood pressure and tachycardia occurred. One such case is shown in figure 4. This effect was always transitory and no vasopressors were needed to restore the blood pressure to normal. Without having a 10 per cent solution of S.C.T.Z. available it is impossible to compare its cardiovascular effects with those of thiopentone.

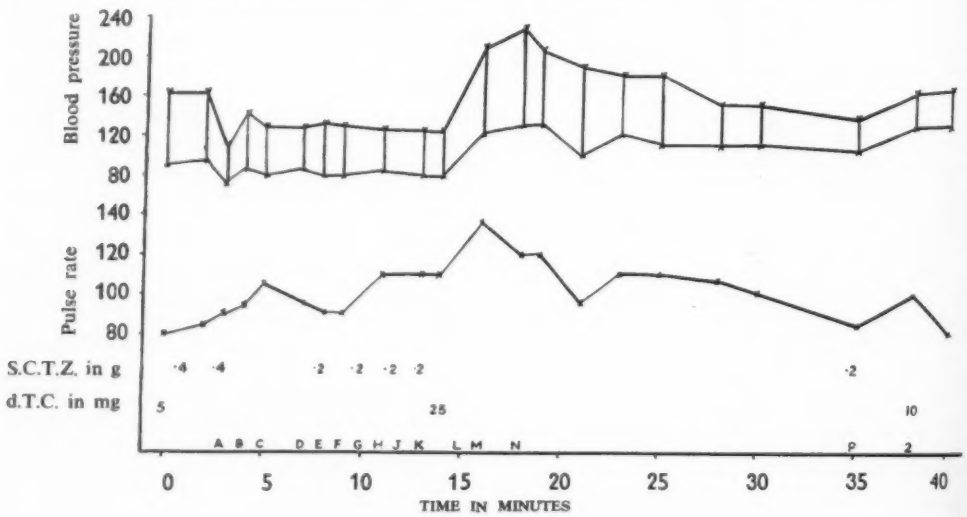

FIG. 3

Blood pressure and pulse changes during induction with S.C.T.Z.
Male aged 51. Operation: Repair of hernia.
Pre-operative medication: Promethazine 25 mg, atropine 0.6 mg.

A = Sleepy.
B = Corneal reflex present.
C = Corneal reflex absent.
D = Corneal reflex returned: moving legs.
E = Objected to injection: moved on stimulation.
F = Mumbling.
G = Objected to supra-orbital pressure.
H = Moving leg.
J = Good jaw tone; still mumbling and moving; winced on injection.
K = Hiccough.
L = Intubated: resisted mildly, moved arms. Inflated with N_2O—O_2.
M = Coughed on tube: swallowing.
N = Red line noted along vein of injection.
P = Skin incision: movement of one arm.
Q = Moving arm slightly.
dTC = d-Tubocurarine chloride.

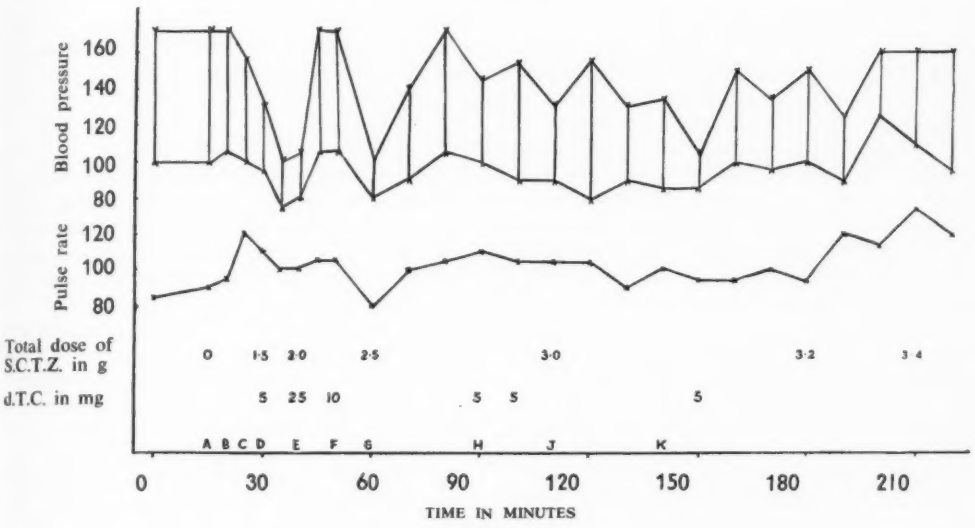

FIG. 4

Blood pressure and pulse changes during operation in a patient anaesthetized with S.C.T.Z.—d-tubocurarine chloride—N_2O—O_2.
Male, aged 57. Operation: Partial gastrectomy.
Pre-operative medication: Promethazine 25 mg, atropine 0.6 mg.

A = Infusion started.
B = Sleepy.
C = Still slight movement.
D = Asleep.
E = Intubation.
F = Skin incision.
G = Moving toes.
H = Hiccough.
J = Some movement.
K = Very marked hiccough.
L = Operation completed. Tachycardia at end of operation due to atropine 1.3 mg, which was given before neostigmine 2.5 mg for reversal of curarization.
dTC = d-Tubocurarine chloride.

Respiration.

Even less data is available on the respiratory effects of S.C.T.Z. than there are on its actions on the circulation. With induction doses employed in this study there seemed to be some increase in both the respiratory rate and tidal volume, but this could always be accounted for by the uneven inductions with frequent struggling. The 15 per cent incidence of coughing and 9 per cent incidence of hiccough following induction must be considered in the light of the fact that patients may have been too lightly anaesthetized at the time. Laryngospasm occurred in one case and later during the operation in the same case there was a decided suspicion of bronchospasm. On the whole, the incidence of untoward complications of respiration were unduly high with S.C.T.Z.

Interaction with other drugs.

S.C.T.Z. appeared to be less synergistic with the volatile narcotic and analgesics than thiopentone. This also applied to the muscle relaxants. No cases of prolonged apnoea or difficult reversal occurred in this series. The ability of d-tubocurarine chloride to "smooth out difficulties" in an abdominal case seemed to be distinctly less after S.C.T.Z.

OVERALL SURVEY

Some aspects of the quality of anaesthesia produced by S.C.T.Z. in the 33 cases in this study are shown in table V. There is no doubt that, with the dose and techniques used in this trial, the drug is definitely inferior to thiopentone.

Attention is drawn to the large volume of the 2 per cent solution used. These varied from 15

to 210 ml. At one time during the trial it was felt that the dilute solution (in relation to the potency of the drug) as compared with thiopentone might have been at least part of the cause of the trouble. To test this hypothesis eight unselected consecutive patients were anaesthetized by the author using a 1 per cent solution of thiopentone. Apart from the expected nuisance of having to handle several 20-ml syringes, no difficulties attributable to the drug occurred in any of these cases. It thus seems unlikely that the form of presentation is the cause of the uneven anaesthesia with S.C.T.Z.

DISCUSSION

An Annotation (1957) refers to S.C.T.Z. as "producing sleep without any degree of analgesia or anaesthesia". This description is fully borne out by the experiences described above. It was unbelievably difficult to produce any resemblance to surgical anaesthesia in some of these patients who were undoubtedly "asleep". This work shows that the terms "sleep" and "anaesthesia" are by no means synonymous, and excellent results reported with nitrous oxide-oxygen show that its action must be more widespread than the simple production of unconsciousness. The importance of some degree of analgesia may be inferred from this study. An alternative explanation of the unsatisfactory results achieved with S.C.T.Z. has already been suggested, namely some stimulant or convulsive action of the drug.

Whatever be the ultimate explanation, it is obvious that S.C.T.Z. has no place in present-day anaesthesia. It fulfils none of the criteria for a satisfactory intravenous agent (Dundee, 1956).

One is always interested in a new type of narcotic, and it is only by examining new drugs that one can expect to advance in the field of intravenous anaesthesia. The concept that narcosis can be produced by part of a vitamin molecule is a new one, and is surprising in light of findings which show the analeptic action of the vitamin B complex (Gould, 1953). Evidence is increasing to show that changing a single atom can completely reverse the action of a complex molecule. An example, well known to anaesthetists, is the conversion of some barbiturates to thiobarbiturates, changing a narcotic drug to a convulsant. It is hoped that further study will be carried out on the thiazole fraction of vitamin B_1, as a simple structural change may produce a more satisfactory anaesthetic agent.

SUMMARY AND CONCLUSIONS

Experimental work has shown that the thiazole fraction of thiamine chlorohydrate is a cerebral depressant as compared with the pyrimidine fraction. S.C.T.Z., a derivative of this thiazole fraction, has been used as an intravenous anaesthetic in 40 cases.

Results show that S.C.T.Z. is not a satisfactory agent for induction or maintenance of anaesthesia. It appears to be completely devoid of analgesic action and, despite its ability to produce sleep, it may have some stimulant action.

The experience obtained on this study has impressed the author with the importance of analgesia in the state of surgical anaesthesia.

ACKNOWLEDGMENTS

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THE TREATMENT OF ACUTE RESPIRATORY INFECTION IN INFANTS

BY

H. I. ARMSTRONG NISBET

Alder Hey Children's Hospital, Liverpool, England

AND

FRANK WILSON

Alder Hey Children's Hospital and Royal Liverpool Children's Hospital, Liverpool, England

THE mortality from acute respiratory infection in infants has been considerably reduced in recent years by the advent of antibiotic therapy. The application of new knowledge concerning fluid balance and feeding, together with advances in the nursing care, and attention to such factors as temperature, posture and humidity of the atmosphere have played important roles in reducing mortality.

Despite this progress, a certain proportion of cases still fails to respond to treatment. Such may be the case where antibiotics are used empirically or in inadequate dosage. Certain infections appear to be resistant to all antibiotic therapy. In some infants in whom there is a paucity of physical and radiological signs, the severity of the condition may not be fully appreciated. Treatment may then be delayed until the development of an obvious severe bronchopneumonia with cyanosis, dehydration and extreme toxaemia. Hypoxia and toxaemia lead to depression of the cough reflex. In such circumstances failure to clear secretions from the air passages results in severe respiratory obstruction.

The purpose of this paper is to show how it is possible to re-establish an adequate airway and improve aeration of the lungs. A series of cases is presented treated by methods that have been evolved using standard equipment readily available in all hospitals.

PRINCIPLES OF TREATMENT

The Relief of Respiratory Insufficiency

Respiratory insufficiency exists where gaseous exchange between the lungs and the blood is less than that between the tissues and the blood—that is, where external respiration cannot keep pace with internal respiration (Woolmer, 1956). The infant's own efforts towards increasing exchange, by increased respiratory rate and effort, are demonstrably inefficient as they inevitably increase oxygen demands.

This discrepancy between oxygen supply and oxygen demand can be relieved in two ways.

(*a*) By increasing gaseous exchange.

(*b*) By reducing oxygen demands.

Increased Gaseous Exchange.

This may be effected by:

Removal of obstructing secretions.

(*a*) By suction applied to the nose, mouth and pharynx.

(*b*) By suction applied to the lower respiratory tract via an endotracheal tube, a bronchoscope or a tracheotomy tube.

The necessity to remove secretions which obstruct the air passage is well recognized in the operating theatre, and in the management of anterior poliomyelitis, tetanus and many varieties of coma. There is less appreciation of the possible effects of mechanical obstruction arising in the infant's airway during the course of acute respiratory infections.

The value of oxygen therapy must be severely limited if it cannot reach the alveoli. Similarly, antibiotics, although invaluable, will do little good unless the airway remains adequate long enough for the patient to benefit from their action.

Re-expansion of collapsed segments.

(*a*) By suction through an endotracheal tube or bronchoscope.

(*b*) By the use of positive pressure after suction.

(*c*) By aspiration of pus and/or air from the pleural cavity.

(*d*) By suitable posture.

Restoration of function to areas of lung by these means must inevitably increase gaseous exchange.

Reduction of deadspace.

(*a*) By endotracheal intubation.

(*b*) By tracheotomy.

Suitable posture.

It has been shown that posture affects:

(*a*) the relative ease with which the various lung segments expand (Jackson Rees, 1958);

(*b*) overall compliance (Attinger, Herschfus and Segal, 1956);

(*c*) the efficient drainage of secretions from the bronchial tree (Quinn and Mayer 1929; McLaurin, 1934).

Reduction of Oxygen Demands

This may be achieved by:

Re-establishment of the airway, using any or all of the methods above.

Since hypoxia and carbon dioxide retention in certain degrees provide the stimuli for the increase in respiratory work, removal of these stimuli by adequate aeration of the lung will reduce effort.

Removal of secretions which increase the resistance to the flow of gases in the air passages must reduce energy requirements.

Respiratory obstruction, by causing increased intrathoracic negative pressure, may facilitate the formation of transudate. This in turn may result in limitation of gaseous exchange, a decrease in compliance and an increase in respiratory work in addition to impairing the diffusion of gases across the membrane.

Use of assisted or controlled respiration.

Judicious use of sedatives.

Avoidance of respiratory stimulants, which must increase the metabolic rate and oxygen demand.

Maintenance of Nutrition and Hydration

This paper is primarily concerned with the application of the principles enumerated above. Nevertheless, the maintenance of nutrition and hydration remains an essential aspect of treatment.

Dehydration results from respiratory distress and toxaemia, which impair the ability to feed adequately. The immature kidneys (Rickham, 1957) function even less efficiently as the high "volume obligatoire" required by the infant is not readily available. Acid-base balance in the blood is impaired not only by faulty ventilation, but by poor renal compensation.

Feeding may be maintained by a catheter inserted into the stomach. It is preferable that, where possible, this should be passed through the mouth, thus leaving the nasal passages clear. The presence of an endotracheal tube in the oropharnyx precludes normal feeding, but as these children are so ill that they will not feed by mouth in any case, this is of little consequence. In such circumstances, feeding by tube becomes essential. Some additional benefit may be derived from the removal of air and gas from the stomach, thus reducing the work of the diaphragm.

The Early Institution of Efficient Antibiotic Therapy

A detailed discussion of antibiotic therapy is outside the scope of this paper, but it must be appreciated that, if this is to be efficient, reliable information regarding the nature of the infecting organism must be obtained early in the course of the disease.

The empirical use of drugs to which the organism may subsequently be proved insensitive is unavoidable in the early stages of treatment. However, secretions aspirated from the trachea and bronchi provide the bacteriologist with far more reliable diagnostic material than do either throat or laryngeal swabs. Thus endotracheal intubation and suction may facilitate the early use of a suitable antibiotic.

MODE OF TREATMENT

It is desirable that the atmosphere, posture, humidity and temperature should be readily controllable and that the respiratory movements should be easily observed. Such conditions may best be achieved where the infants are nursed naked in incubators.

Restoration of the airway by intubation and suction forms the essential feature of the treatment in all cases we describe. In some instances, intubation has had to be repeated many times and in others it has been necessary to leave an endotracheal tube in position for prolonged periods. Controlled respiration has been found to be beneficial where exhaustion has been so severe as to render ventilation inadequate. On occasion sedation has proved helpful. Where secretions have been particularly tenacious, streptokinase has been used. Certain of our cases have required bronchoscopy and in others tracheotomy has been necessary. These aspects of treatment require some detailed description.

Endotracheal Intubation

When severe respiratory embarrassment results from acute infection in infancy, the indications for intubation are:

(*a*) Where obstructing secretions cannot be cleared effectively in the normal way, that is, where there is an ineffective cough.

(*b*) Where the child is too ill to maintain adequate ventilation by its own unaided efforts.

The presence of an efficient cough mechanism is undoubtedly the most effective way of removing secretions. It follows that intubation is seldom necessary where this exists. On the other hand, failure to cough effectively, as evidenced by the audible accumulation of secretions in the larger air passages, or by the presence of atelectasis, will present a strong indication for intubation.

In such circumstances, the introduction of an endotracheal tube offers several advantages.

(*a*) Mechanical obstructions presented by the relaxed tongue, blocked nares and pharyngeal secretions are overcome.

(*b*) Repeated endotracheal and endobronchial toilets can be carried out by suction through the tube. Owing to the more vertical descent of the right bronchus, toilet of the right bronchial tree is easily performed, while it may be necessary to resort to bronchoscopy to clear the left bronchus.

(*c*) Deadspace is reduced. If the tidal volume of an infant is 10 ml and the deadspace is 5 ml, the effective tidal volume which takes part in respiratory exchange will be 5 ml. If, however, the tidal volume is only 6 ml, the effective tidal volume will be only 1 ml.

Intubation with an 00 gauge endotracheal tube reduces the deadspace above the subglottic region from 5 ml to 1 ml. Thus the effective tidal volume will be greatly increased with a corresponding reduction in tachypnoea.

Although an endotracheal tube offers increased resistance to breathing in a normal infant, where this resistance is already high due to the presence of secretions in the air passages it is likely that the removal of these secretions by intubation and suction will actually effect a reduction in resistance. Our cases have shown a marked fall in respiratory rate following such treatment. This would seem to indicate a diminution in respiratory effort and therefore in oxygen demand.

Technique.

A sterile tray containing apparatus necessary for intubation should now be standard equipment in the medical wards of children's hospitals.

Intubation of an infant in extremis is not technically difficult. Any material present in the pharynx is quickly removed by suction. The laryngoscope is gently inserted, advanced down the pharynx into the oesophagus and withdrawn until the tip catches the epiglottis, when the larynx slides into view. A sterile Magill tube is now introduced. This should be of too small a bore rather than too large, and should pass into the larynx to a point just below the vocal cords. The length can roughly be estimated by measuring one and a half times from the corner of the mouth to the lobe of the ear. If the tube is too long, it will enter the right bronchus, thus adding to the respiratory embarrassment. Size 00 Magill tubes are used in most cases. Kinking of the tube will occur less readily if a firm tube is selected.

While infants up to two or three weeks of age, and those who are moribund present little difficulty, it may be wiser to produce muscular relaxation in older and more active children if intubation is to be accomplished with a minimum of trauma. Intravenous injection of 5–10 mg of suxamethonium will cause complete paralysis and thereafter intubation may be performed with ease following inflation of the lungs with oxygen from a face mask.

Following intubation a fine no. 3 Jacques rubber catheter, from which the end has been removed, is introduced into the trachea. Suction is applied and whatever secretion present is removed. As this forms valuable diagnostic material, the contents of the sterile catheter mount should be sent for investigation.

The lungs are now inflated with oxygen, the tube being connected to the T-piece circuit as shown in figures 1 and 2. If the lungs fail to expand when gentle pressure is applied to the bag, suction should be repeated until inflation is possible.

Further Management.

The subsequent treatment depends upon the child's response. Where the condition is obviously much improved, with rapid return of normal colour to the mucous membranes and when coughing, stimulated by the presence of the tube, is active, then the tube should be removed. After inflation of the lungs with oxygen and careful pharyngeal suction, the tube is withdrawn in one smooth rapid movement. Auscultation near the mouth confirms that the airway is clear and that no laryngeal spasm exists.

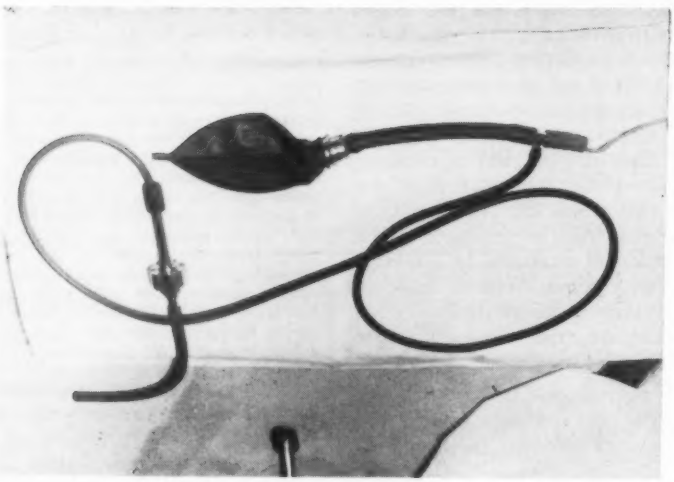

FIG. 1
Rees's modification of Ayre's T-piece circuit with Venturi device for the entrainment of air.
A humidifier is normally interposed between the Venturi device and the T-piece.

Careful observation of the infant's condition is essential, as the lung segments may well collapse repeatedly. Special attention should be paid to the presence or absence of an effective cough and to the nature of air entry on auscultation near the mouth or nose. This latter measure may give an early indication of the gradual accumulation of secretions. Repeated examination of the chest is necessary as the signs may vary markedly from hour to hour. Careful attention should be paid to the state of hydration. Radiographic and biochemical investigations should not be delayed.

Repeated Intubation.

Should secretions continue to accumulate in the absence of an effective cough, repeated intubation and suction may well be required. It is desirable that all manoeuvres should be performed as gently as possible and that trauma to the larynx be avoided. A small dose of suxamethonium may help greatly to attain this aim.

In certain cases we have experienced considerable difficulty in distinguishing between areas of collapse and consolidation. If the air entry to an area of the lung should suddenly become markedly diminished then the diagnosis is usually obvious. The presence of moist sounds, in association with an area of diminished air entry may also suggest that accumulated secretions have resulted in collapse. On the other hand, the absence of moist sounds in such an instance is no proof that the signs are due to consolidation. We have been surprised to find that some areas thought clinically to show consolidation have been re-aerated following suction and positive pressure. Where such uncertainty exists intubation and suction may be a useful diagnostic procedure.

Prolonged Intubation.

Where the child is exhausted and respiration is inadequate to maintain oxygenation, the endotracheal tube must perforce be retained and controlled respiration instituted.

In such a situation, expert, detailed and constant nursing care is essential. The nursing staff has played an invaluable part in the management of these cases. The organization of specialized respiratory units for the management of these cases would seem desirable.

The nurse should be taught to watch and listen for any change in the character of breathing. The

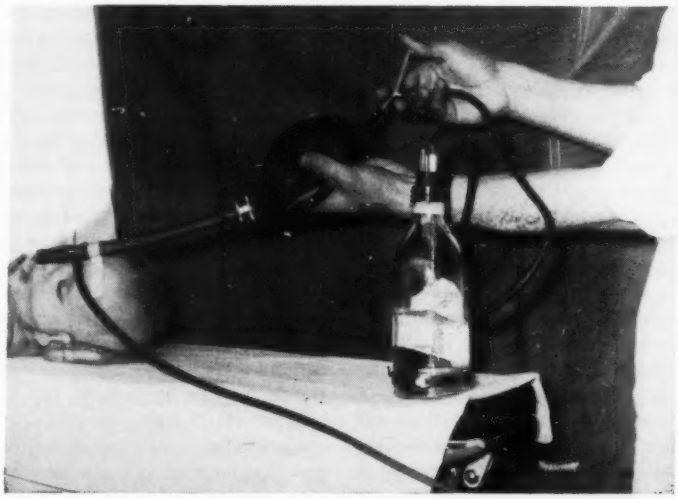

FIG. 2

Rees's modification of Ayre's T-piece circuit in use, with safety device.

A green rubber bag, as supplied by B.O.C., is connected to the T-piece circuit. Into the "tail" of this bag is inserted a Y-shaped glass connection. The second limb of this connection is attached to the glass tubing in a transfusion bottle, which is half full of water. The glass tubing dips well below the surface of the water.

"Inspiration" is effected by closing the third limb of the Y-shaped connection with the thumb of one hand, while the thumb of the other compresses the bag. The pressure in the circuit is then limited by the escape of gases through the limb of the Y connection attached to the transfusion bottle. "Expiration" is effected by releasing the pressure on the bag and removing the thumb from the limb of the Y connection.

circuit should be demonstrated and special emphasis laid upon all the possible means by which the airway may be blocked and the ways in which it may be restored.

Sudden onset of respiratory distress, with intercostal recession, cyanosis and diminished air flow through the tube, requires prompt attention. The smaller sized endotracheal tubes are thin walled and may kink. Such difficulties may be prevented if a reasonably firm tube is secured in the midline, the connection lying between the teeth or gums, where it cannot be blocked by biting. A gag made from a cut-down Guedel's airway may be useful in this connection. Careful packing of the mouth and pharynx with a lightly oiled gauze pack also limits the tendency of the tube to kink. Failure to make a firm connection between the tube and its metal connection may lead to inhalation of the tube.

Should it be necessary to retain the tube in position for periods of longer than twelve hours, it is advisable to change it frequently in order to avoid blockage by inspissated secretions.

Suction

The majority of these children suffer from a generalized infection of the respiratory passages. Copious secretions may accumulate in the nose, pharynx, trachea and bronchi. As infants show a predilection for nasal breathing, it is desirable that the patency of the nasal passages should be maintained. Furthermore, if nasal secretions are not efficiently removed they will collect in the pharynx, giving rise to a mechanical obstruction. Pharyngeal suction, therefore, is a valuable thera-

peutic measure. It should be performed hourly, preferably before the child is due to be fed, in order to avoid regurgitation. Even when an endotracheal tube is in position, these measures should not be neglected. An adequate exposure is necessary and is easily obtained by depressing the tongue with a sterile spatula or spoon handle without causing trauma to the palate or posterior pharyngeal wall.

Suction through an endotracheal tube is not without certain hazards, and should only be performed by those who have received instruction. Care should be taken to ensure that the catheters are sterilized by boiling before and after use. Sterilization by means of solutions or by formalin vapour cannot be too strongly condemned. A firm rubber catheter of a thickness such as will permit the passage of air between itself and the wall of the endotracheal tube should be passed as far down the bronchial tree as possible. Care is necessary to avoid trauma to the tracheal wall and the catheter should be firmly compressed as it passes down. Suction is then applied as the catheter is withdrawn, removing secretions on the way. Failure to observe these precautions may result in considerable collapse of the lungs. Following suction, inflation of the lungs with oxygen should always be performed, further to minimize this danger. Some measure of restraint is advisable in the use of suction. It should only be applied where secretions are thought to exist and not as a diagnostic test of their presence or absence. Strict attention should be paid to asepsis.

Controlled Respiration

Controlled positive pressure respiration may produce certain adverse effects on the cardiovascular dynamics of adult subjects. It is believed that, in healthy infants, such effects are minimal (Rees, 1958). This is less likely to be true where circulatory collapse exists due to toxaemia, dehydration or the effects of prolonged hypoxia.

When the tidal volume is inadequate to maintain oxygenation, however, or the child is apnoeic, there is little choice but to control respiration. Beneficial effects should result from the improved ventilation and the reduction in oxygen demand consequent to diminished respiratory work. It is unlikely that positive pressure respiration will injure a normal lung provided that it is performed with care. Rees (1958) states that quite a high negative intrathoracic pressure may be reached in infants. The negative intrathoracic pressure produced by diaphragmatic movement is inversely proportional to the radius of the domes. As this radius is small in infants, they can produce pressures in the region of -45 cm H_2O. Similarly, high positive intrathoracic pressures are known to be developed in the act of coughing—pressures far in excess of those used in positive pressure respiration.

The Rees modification of Ayre's T-piece circuit is shown in figure 1. As it stands, it is not suitable for use by untrained personnel. A further modification, described in figure 2, limits the pressure which may be applied to the lungs by manual inflation of the bag.

Controlled respiration with this equipment may be carried out safely by the nursing staff, provided that adequate instruction is given. Points to stress are that the bag must not be allowed to fill completely, being partially grasped in the ball of the hand, while pressure to inflate is exerted by the thumb. Pressure should be gentle and sufficient to ventilate adequately as judged by the movements of the chest. The pressure during the expiratory phase should be zero.

Ayre (1956) states that in clinical practice a fresh gas inflow of $1\frac{1}{2}$–2 times the minute volume of the patient will ensure that there is no rebreathing.

Humidification

Humidification of the atmosphere is essential in all cases. Marshall and Spalding (1953) state that the aim should always be 100 per cent humidity. This is difficult to obtain where the incubators are frequently opened for feeding, auscultation and routine nursing care. Incubators should be opened, therefore, as seldom as possible, both to preserve the oxygenated humidified atmosphere and to avoid falls in temperature which may be serious in collapsed hypothermic infants. Where an endotracheal or a tracheotomy tube is in place, failure to provide adequate humidification will lead rapidly to the encrustation of secretions. In both these instances, the mouth and nose, which normally add most of the water vapour to the inspired air, are by-passed.

It is wise, therefore, to keep humidity settings

on the incubators at the maximum. Clinical impressions are that the addition of alevaire to the atmosphere is useful.

If controlled respiration is required, 100 per cent humidity can only be obtained by the use of a humidifier such as the "Radcliffe". Where this is not available the gases may be bubbled through water bottles in which the bubbles are broken up by passing through gauze or sponge. This method gives a humidity below the desired maximum (Marshall and Spalding, 1953).

The Atmosphere

It is generally agreed that prolonged inhalation of high concentrations of oxygen is undesirable. The concentration in many incubators, however, seldom reaches 50 per cent (Rickham, 1957). Where incubators are more airtight, it seems advisable that alevaire should be vaporized by air and an appropriate percentage of oxygen added to the atmosphere through a separate inlet. Controlled respiration with 100 per cent oxygen is likewise to be avoided. The introduction of a venturi injector device into the T-piece circuit enables the entrainment of air, so that the relative concentration of air and oxygen may be varied as desired.

Position of the Patient

If the child is to make the best use of its respiratory efforts it is desirable:

(*a*) That the inhalation of material from the nose, mouth and pharynx should be avoided.
(*b*) That the position should be such as will encourage the drainage of secretions from affected segments.
(*c*) That the position should allow the infant to ventilate its lungs with the minimum of effort.

These objectives, unfortunately, are not always compatible.

Most of these children have muco-pus in the nasopharynx. Quinn and Mayer (1929) and McLaurin (1934) have shown the ease with which material from the nose and sinuses may be aspirated into the lungs. The infant's predilection for nasal breathing has already been mentioned. From this the head down position might appear to have certain benefits to offer. Sticky mucus does not drain from the mouth with such facility as liquid vomitus, however, and this position has many disadvantages. Nasal secretions can and should be removed frequently by suction.

James, Brimblecombe and Weston Wells (1952) have shown that atelectasis in lower respiratory infection occurs most frequently in the lower lobes. Most of the cases in this large series, however, are in an older age group than those with which we have been concerned.

Certain considerations tend to show that the position of choice may be head up. Goodwin (1934) reviewed cases of lipoid pneumonia secondary to aspiration of oily substances. He found that the right lung was more often affected than the left and the upper lobes more frequently than the lower. Rees (1958) states that atelectasis due to secretions is more common in the upper lobes of infants than in the bases. This he ascribes to the abdominal type of respiration and the restricted movement of the upper part of the thoracic cage.

The routine nursing care of changing the child from one side to the other at regular intervals undoubtedly facilitates the drainage of secretions into the larger air passages, from which they may more easily be removed by coughing or by suction. Percussion of the chest wall also assists in this aim.

In respiratory distress there is an increase in respiratory work due to a decrease in compliance and an increase in mechanical resistance. Attinger, Herschfus and Segal (1956) studied a group of adults suffering from various cardiopulmonary diseases. They found that compliance was highest and mechanical resistance lowest in the sitting position. Thus these patients performed less work when sitting than when supine. Positions other than the sitting therefore produce a relatively greater oxygen demand, a condition to be avoided in pulmonary insufficiency.

It may be that these facts are applicable to infants. Certainly marked clinical improvement may be observed when they are made to sit up. This posture should allow the diaphragm to act at a better mechanical advantage. The infant must not be allowed to slump forward in a nest of pillows, however, or this advantage is lost.

In view of these considerations we have elected to treat these cases with the head end of the bed steeply raised on blocks, or with the incubator tray suitably tilted. The children are turned from side to side at regular intervals and are not encumbered by pillows.

Sedation

It may be considered that sedation in these cases is inadvisable, in view of the ever present dangers of hypoxia and carbon dioxide retention. Gaisford and Lightwood (1953) have favoured the use of pethidine in certain conditions of respiratory distress. We have found that, in several instances, a dose of 0.2 mg per lb. (0.45 mg/kg), by intramuscular injection, has had a quietening effect in restless infants. In such amounts it does not appear to cause significant respiratory depression and by virtue of its sedative effect, reduces oxygen demand.

Avoidance of Respiratory Stimulants

While certain concentrations of carbon dioxide stimulate respiration it seems likely that raised levels already exist in the blood where ventilation is defective (Goodman and Gillman, 1955). Further increase in the concentration in the inspired atmosphere may lead to respiratory depression.

It has been shown by Alschultz and Sulzbach (1947) and McDonald and Simonson (1953) that changes in blood carbon dioxide level affect the adult electrocardiogram. Reversible changes similar to those seen in ischaemic heart disease have been described by Pitman and Wilson (1955) in cases of respiratory embarrassment with carbon dioxide retention. It would be interesting to know if such changes occur in infants.

Whether a stimulant effect, obtained by carbon dioxide or by the use of such drugs as niketha-mide, is desirable in an exhausted child may be doubted, in view of the increased oxygen demand which must inevitably result.

Temperature Control

It has been shown that adults adjust their rate and depth of breathing so that respiration is accomplished with a minimum of effort (Otis, Fenn and Rahn, 1950; McIlroy, Marshall and Christie, 1954). The theoretical minimum of effort in the newborn is thought to occur at a respiratory rate of 37 per minute (Cook et al., 1957). Work done increases as the rate rises above this figure and the metabolic rate may attain phenomenal levels.

From these considerations, it may be surmised that respiratory distress in infancy calls for a much greater increase in effort than in adult life. Reference has been made elsewhere (Freier et al., 1957) to the pyrexia and exhaustion which may accompany increased respiratory effort. In two cases of hyaline membrane syndrome described by Cook and his colleagues (1957) the metabolic rate was increased by 400 per cent. As mechanical efficiency is low, a high proportion of the energy used in the increased respiratory effort will appear in the form of heat. Small wonder that the distressed infant, with its poorly developed heat regulating mechanism, commonly develops hyperpyrexia, which may be accompanied by convulsions.

It is surprising, therefore, to find that infants with marked pyrexia are still commonly nursed under layers of clothes and blankets, or in incubators at high temperatures. Such treatment can only have the effect of raising the metabolic rate and oxygen demand.

Where the child is collapsed and exhausted, however, the temperature rapidly falls, sometimes to levels well below 90°F. In such circumstances it is essential to maintain the temperature of the incubator at a high level. Thus the number of occasions when it is opened for nursing purposes should be kept to a minimum.

Bronchoscopy and Tracheotomy

In many cases we have found it possible to re-expand the lungs simply by intubation and suction followed by positive pressure. The right lung responds well to this treatment but in many cases the left lung also has benefited to such an extent that bronchoscopy has not been required. Where the response has been less satisfactory bronchoscopy has proved useful.

Modern thought does not subscribe to the view that tracheotomy in infants invariably leads to a fatal outcome. A planned operation in theatre, followed by judicious use of antibiotics, devoted nursing care, atmospheres of high humidity and careful endotracheal toilet, gives even the youngest child a fair chance of survival.

It is not proposed to discuss the management of tracheotomy, but some reference is made to the subject later in the comment on case history no. 8.

Streptokinase and Streptodornase

In certain cases, where mechanical obstruction due to tenacious or crusted material was causing

TABLE

Ref.	No.	Sex	Age	Birth weight	Nature of disease	Presenting features	Outline of treatment
C.F.	10	Female	2 weeks	8 lb. (3.5 kg)	Bronchiolitis.	Cyanosis, rib recession, periods of apnoea, pallor. Poor air entry, right lung and left base.	Intubation and suction.
P.H.	11	Male	5 weeks	5 lb. 6 oz. (2.5 kg)	Bronchopneumonia.	Pallor. Cyanosis. Apnoea. Laryngeal oedema. Massive accumulation of secretions. No air entry left lung.	Repeated intuba and suction. Prolonged intub Controlled respi Tracheotomy.
G.M.	12	Female	8 weeks	6 lb. (2.75 kg)	Bronchopneumonia.	Grey, long periods of apnoea. Poor air entry.	Intubation and suction.
N.B.	13	Male	10 weeks	8 lb. (3.5 kg)	Bronchiolitis.	Extreme dyspnoea, cyanosis. Poor air entry right lung and coarse crepitations over left lung.	Intubation and suction. Bronchoscopy.
L.G.	14	Female	3 weeks	5 lb. 9 oz. (2.5 kg)	Bronchiolitis.	Extreme dyspnoea, cyanosis, poor air entry throughout.	Intubation and suction.
A.H.	15	Female	6 weeks	7 lb. 3 oz. (3.25 kg)	Bronchitis.	Cyanosis. Respiratory distress. Accumulation of secretions in pharynx.	Pharyngeal suct Postural draina
C.D.	16	Female	2 weeks	5 lb. 13 oz. (2.75 kg)	Bronchiolitis.	Cyanosis. Massive accumulation of secretions. Poor air entry all areas.	Repeated intuba and suction. Bronchoscopy.
R.F.	17	Male	6 weeks	5 lb. (2.25 kg)	Bronchopneumonia.	Cyanosis. Gasping respirations. No air entry except at left apex. Respiratory rate 96 per minute.	Repeated intuba and suction.
C.L.D.	18	Female	20 months	7 lb. 4 oz. (3.25 kg)	Acute laryngitis.	Stridor, cyanosis, poor air entry in all areas, restlessness, and confusion.	Oxygen therapy intubation, tracheotomy, humidification.

TABLE I—*Continued*

ng	Outline of treatment	Immediate response	Subsequent course.	Organisms isolated	A
reces- of or. Poor ht lung	Intubation and suction.	Good.	Gradual improvement.	Staph. pyogenes.	P S E
osis. yngeal ssive o of o air ng.	Repeated intubation and suction. Prolonged intubation. Controlled respiration. Tracheotomy.	Good.	Gradual improvement.	None.	P S E
eriods oor air	Intubation and suction.	Good.	Gradual improvement.	Staph. pyogenes.	E S
noea, or air ung and ations g.	Intubation and suction. Bronchoscopy.	Good.	Gradual improvement.	B. coli. Streptococcus haemolyticus.	P E
noea, r air hout.	Intubation and suction.	Good.	Gradual improvement.	B. coli.	A
distress. of	Pharyngeal suction. Postural drainage.	Good.	Improvement.	Staph. pyogenes.	E S
assive of or air s.	Repeated intubation. and suction. Bronchoscopy.	Good.	Gradual improvement.	B. Coli.	P S
ping No air at left atory inute.	Repeated intubation and suction.	Respiratory rate dropped to 50 per minute within half an hour.	Gradual improvement.	Nil.	O an T P S E A
osis, y in all ness,	Oxygen therapy, intubation, tracheotomy, humidification.	Good.	Rapid improvement.	Staph. pyogenes.	P S

sms d	Antibiotics used	Complications	Fate
es.	Penicillin. Streptomycin. Erythromycin.	Congestive failure.	Survived.
	Penicillin. Streptomycin. Erythromycin.	Laryngeal oedema.	Survived.
es.	Erythromycin. Streptomycin.	Nil.	Survived.
coccus rticus.	Penicillin. Erythromycin.	Congestive failure. Congenital heart disease. ? Infundibular stenosis.	Survived. For cardiac surgery.
	Achromycin.	Prematurity.	Survived.
s.	Erythromycin. Streptomycin.	——	Survived.
	Penicillin. Streptomycin.	Prematurity. Congestive failure.	Survived.
	Oral penicillin and oral Terramycin. Penicillin. Streptomycin. Erythromycin. Aureomycin.	Nil.	Survived.
s.	Penicillin. Streptomycin.	Nil.	Survived.

Ref.	No.	Sex	Age	Birth weight	Nature of disease	Presenting features
C.K.	1	Female	4 weeks	5 lb. 9 oz. (2.5 kg)	Bronchopneumonia.	Pallor. Hypothermia. Circulatory collapse. Cyanosis, long periods of apnoea. Poor air entry in all areas.
G.W.	2	Male	6 weeks	8 lb. 5 oz. (3.75 kg)	Bronchitis.	Cyanosis, gasping respirations. Poor air entry all areas.
I.E.	3	Male	5 weeks	8 lb. (3.5 kg)	Staphylococcal pneumonia.	Pallor, cyanosis, dyspnoea. Poor air entry, especially left lung. Laryngeal oedema.
J.M.	4	Male	5 weeks	3 lb. 8 oz. (1.5 kg)	Bronchiolitis.	Pallor, cyanosis, dyspnoea, periods of apnoea. Poor air entry throughout. Moderate laryngeal oedema.
D.L.	5	Male	6 weeks	4 lb. 8 oz. (2 kg)	Bronchiolitis.	Grey, long periods of apnoea. Air entry absent in most areas.
C.L.	6 (twin of 5)	Male	6 weeks	4 lb. 8 oz. (2 kg)	Bronchiolitis.	Grey. long periods of apnoea. Poor air entry.
G.S.	7	Female	8 weeks	6 lb. 12 oz. (3 kg)	Bronchopneumonia.	Cyanosis, gasping respirations. Little air entry left side.
E.K.	8	Female	24 weeks	7 lb. 12 oz. (3.5 kg)	Laryngo-tracheal bronchitis.	Laryngeal obstruction.
S.M.	9	Male	7 weeks	3 lb. 8 oz. (1.5 kg)	Bronchiolitis.	Cyanosis, rib recession. Poor air entry. Vomiting.

facing page 426]

TABLE I

Course and Treatment of 18 Cases of Respiratory Infection.

senting atures	Outline of treatment	Immediate response	Subsequent course	On i
r. Hypothermia atory collapse. osis, long s of apnoea. air entry in all	Prolonged intubation. Controlled respiration.	Poor circulatory response in spite of adequate aeration of lungs.	Downhill.	
osis, gasping ations. Poor try all areas.	Repeated intubation and suction.	Good.	Died suddenly.	
, cyanosis, dys- . Poor air especially left Laryngeal na.	Prolonged intubation, and suction. Bronchoscopy. Pleural drainage. Controlled respiration.	Poor circulatory response in spite of improved aeration.	Slow improvement until died suddenly.	
, cyanosis, oea, periods of a. Poor air throughout. rate laryngeal a.	Repeated intubation and suction. Prolonged intubation Bronchoscopy. Controlled respiration. Tracheotomy.	Good.	Periods of apnoea continued. Died suddenly.	
long periods of a. Air entry in most areas.	Intubation and suction. Prolonged intubation. Controlled respiration.	Good.	Periods of apnoea continued. Died suddenly.	
long periods of a. Poor air	Intubation and suction. Prolonged intubation. Controlled respiration.	Good.	Gradual improvement.	
osis, gasping ations. Little try left side.	Repeated intubation and suction.	Good.	Gradual improvement.	
geal ction.	Tracheotomy and suction. Repeated bronchoscopy.	Good.	Gradual improvement.	
osis, rib reces- Poor air entry. ing.	Intubation and suction. Bronchoscopy.	Good.	Gradual improvement.	

TABLE I

of 18 Cases of Respiratory Infection.

of t	Immediate response	Subsequent course	Organisms isolated	Antibiotics used	Complications	Fate
ntubation. spiration.	Poor circulatory response in spite of adequate aeration of lungs.	Downhill.	B. coli.	Erythromycin.	Prematurity. Dehydration. Diarrhoea. Circulatory failure. Patent ductus arteriosus.	Died.
ubation	Good.	Died suddenly.	B. coli.	Erythromycin. Streptomycin.	Complete obstruction of airway by secretions.	Died
ntubation, y. age. spiration.	Poor circulatory response in spite of improved aeration.	Slow improvement until died suddenly.	Staph. pyogenes.	Penicillin. Streptomycin Erythromycin.	Bronchopleural fistula. Purulent pericarditis. Acute bacterial endocarditis. Complete obstruction by secretions.	Died.
ubation ntubation y. spiration.	Good.	Periods of apnoea continued. Died suddenly.	B. coli. Staph. pyogenes. Pneumococci.	Penicillin. Streptomycin. Erythromycin.	Prematurity. Laryngeal oedema. Cerebral oedema.	Died.
d tubation. spiration.	Good.	Periods of apnoea continued. Died suddenly.	Staph. pyogenes.	Chloramphenicol.	Complete obstruction of airway due to secretions.	Died.
nd suc- ntubation. espiration.	Good.	Gradual improvement.	None.	Erythromycin. Streptomycin.	Gastroenteritis.	Survived.
ubation	Good.	Gradual improvement.	None.	Erythromycin.	Congenital heart disease, ventricular septal defect.	Survived.
and eated y.	Good.	Gradual improvement.	None.	Erythromycin. Streptomycin.	Encrustation of secretions.	Survived.
nd y.	Good.	Gradual improvement.	Staph. pyogenes.	Erythromycin. Streptomycin.	Prematurity.	Survived.

[P.T.O.

alarm, we have found these preparations valuable when instilled into the bronchial tree. In other cases, liquefaction of pus has appeared to cause rapid spread of infection. It may therefore be advisable to wait until systemic antibiotics have had time to be effective before using these substances.

TYPES OF CASES

From a therapeutic viewpoint it is desirable to define several broad groups of clinical conditions.

(1) Upper respiratory tract infection may predominate, as in cases of laryngotracheal bronchitis, where subglottic oedema may be sufficiently severe to call for early tracheotomy.

(2) Bronchitis or bronchopneumonia may exist where copious, sticky, muco-purulent secretions remain uncleared from the larger air passages and may be followed by atelectasis, consolidation or abscess formation. This group presents the anaesthetist with the most promising field for intervention.

(3) Where the obstructing secretions are situated mainly in the smaller bronchioles, efforts to remove them are likely to be less rewarding. Repeated suction may be required to remove them as they are extruded into the larger bronchi. The effort entailed in maintaining ventilation in these cases of bronchiolitis is very great and many have required prolonged intubation and controlled respiration.

(4) Abscess formation is frequent in staphylococcal infections. Such lesions may rupture into a bronchus, causing sudden acute respiratory obstruction. Not uncommonly, however, they rupture into the pleural cavity, causing a pyopneumothorax, a condition which calls for careful management.

CASE HISTORIES

In view of the urgent problem presented by the cyanotic, gasping, collapsed infant, we have had little choice in the cases we have treated. Some children are moribund on admission. Seven cases, not included in our series, have died before we could reach them, even though the delay was short. In some, postmortem examination has revealed the presence of associated lesions, as can be seen from table I.

Controlled investigation has not been possible in these circumstances and early investigations by such means as radiography have often been precluded. Results are therefore difficult to assess by any means other than by clinical examination.

The principal features of eighteen cases of acute respiratory infection are indicated in table I. In order to avoid tiresome repetition, certain of these cases which demonstrate particular methods of treatment are presented and only two are described in detail. In this series there have been five deaths, which will be discussed collectively.

Case No. 15.

Pharyngeal Suction and Postural Drainage

A female child aged 6 weeks, birth weight 7 lb. 3 oz. (3.25 kg), was admitted suffering from cyanosis and respiratory distress.

On examination, the child was cyanotic and the respiratory rate was 48 per minute. She made efforts to cough, but was unable to clear the accumulated secretions from the pharynx. Breath sounds were harsh with crepitations throughout both lung fields.

The pharynx was cleared by suction and her colour improved considerably. As she continued to cough, the pharyngeal suction proved sufficient to maintain her airway. She was nursed in the sitting position in an atmosphere of oxygen and alevaire. Postural drainage aided by percussion of the chest was encouraged. She made an uneventful recovery.

Comment. This infant responded well to the usual medical care once the airway had been cleared and maintained. The value of repeated pharyngeal suction was clearly demonstrated.

Case No. 14.

Intubation and Suction

A female child aged 3 weeks, birth weight 5 lb. 9 oz. (2.5 kg), was admitted with a history of "snuffles" and disinclination to feed of several days duration.

On examination she showed cyanosis, dyspnoea and marked rib recession. The breath sounds were harsh, with coarse crepitations at the left base.

On the evening of her admission her condition worsened, with only a temporary response to pharyngeal suction, oxygen and alevaire. She became unconscious with shallow ineffective respirations, poor air entry into all areas of the lungs and periods of apnoea.

Endotracheal intubation was performed without relaxation and a considerable quantity of tenacious sputum removed by suction. Normal colour rapidly returned to the mucous membranes and she coughed strenuously with the tube in place.

Following this procedure, tidal ventilation remained adequate. The air entry improved in all areas and cough remained effective. Further intubation was not required. The child responded satisfactorily to antibiotics and was discharged in due course.

Comment. Where the secretions are tenacious and accumulate in quantity, anoxia will eventually depress the cough reflex. In such a case it is difficult to see any alternative to intubation and suction.

Case No. 17.

Repeated Intubation and Suction

A male child aged 6 weeks, birth weight 5 lb. (2.25 kg), was admitted suffering from cyanosis and respiratory distress. For the three weeks prior to admission he had been treated at home with oral penicillin and terramycin.

Shortly after admission his condition deteriorated. Treatment was continued with penicillin, streptomycin, aureomycin and cortisone. During the next few hours his respiratory rate rose to 96 per minute. He had no air entry except at the left apex.

Intubation was performed without relaxation and 3 ml of blood-stained mucus were aspirated. In the next 2 hours his respiratory rate fell to 50 per minute. During the next 5 days he required daily intubation and suction.

He made an uneventful recovery and was discharged 3 weeks later.

Comment. This case illustrates the fact that respiratory distress may become more severe in spite of antibiotic therapy. When the respiratory obstruction was removed by suction, the respiratory rate fell markedly within half an hour and there was progressive clinical improvement.

Case No. 3.

Prolonged Intubation, Pleural Drainage

A male child aged 5 weeks, birth weight 8 lb. (3.5 kg), was admitted with a history of "snuffles", reluctance to feed and diarrhoea of 24 hours duration.

On examination his colour was good, there was some nasal discharge and scattered rhonchi were heard throughout the lung fields. The heart sounds were normal.

Thirty-six hours after admission the child collapsed before being fed. The skin was pale, mucous membranes blue-grey; rib recession was marked and there was mediastinal shift to the left with no air entry to the left lung. There were prolonged periods of apnoea.

Intubation was performed with the object of re-expanding the left lung. The response to suction was poor and gentle positive pressure was required to maintain ventilation. Bronchoscopy revealed the presence of scanty secretions in both main bronchi which were removed by suction. A loud rough systolic murmur was now evident across the entire praecordium.

As positive pressure resulted in a marked mediastinal shift to the right, the presence of a bronchopleural fistula was suspected. This was confirmed by radiographs which demonstrated a left pyo-pneumothorax.

The child was transferred to theatre, where drainage of the pleural cavity was performed. Following this procedure the child remained pale, blue, and collapsed in spite of the presence of an efficient underwater seal. Respiration still required to be controlled. The loud systolic murmur was still evident. Intramuscular erythromycin was administered.

During the night endotracheal suction was required repeatedly. The tidal exchange improved slowly and it became possible to discontinue controlled respiration.

By the following afternoon the child's condition had greatly improved. He remained pink in the oxygenated and humidified atmosphere of the incubator; tidal ventilation was reasonable and coughing was active. It was deemed advisable to remove the tube, which had by now been in position 24 hours, during which period it had twice been changed.

The following day saw this satisfactory progress continued. The systolic murmur became less marked. That night, however, the child again collapsed. A delay of 8 minutes occurred before intubation, when it was found that the trachea and bronchi were completely blocked by secretions. Inflation of the lungs prior to suction was quite impossible and by the time the airway was re-established the child was dead.

Postmortem examination showed staphylococcal pneumonia with left empyema; purulent pericarditis and acute bacterial endocarditis.

Comments. (1) Positive pressure must be used with caution in those cases where a staphylococcal abscess may have ruptured into the pleura. If the presence of a bronchopleural fistula is suspected, it may be wise to confine treatment to clearing the airway by intubation and suction and then refrain from exerting positive pressure until such time as the surgeon is ready to insert pleural drainage.

(2) It is worthy of note that, in spite of the postmortem findings in the heart, the immediate cause of death in this child was respiratory obstruction due to massive accumulation of secretions, possibly arising from the sudden rupture of a staphylococcal abscess into a bronchus.

(3) Intubation and suction over a period of 24 hours had no ill effect on the larynx or trachea.

Case No. 16.

Prolonged and Repeated Intubation

A female child aged 14 days, birth weight 5 lb. 13 oz. (2.75 kg) was admitted suffering from distressed respiration, cyanotic attacks and inability to suck at the breast.

February 6, 1958.

11 p.m. On examination the temperature was 95°F, the pulse and respiratory rates were 142 and 64 per minute respectively. The infant was cyanosed and had marked respiratory distress with intercostal recession.

Air entry was absent except over the right upper zone. A marked systolic murmur was audible over the praecordium.

A laryngoscope was inserted into the pharynx and purulent secretions were seen to well up from the laryngeal aperture. The aryepiglottic folds were markedly inflamed.

An endotracheal tube was inserted and 3–4 ml of thick yellow pus were aspirated. Air entry was immediately evident over the right lung except at the base. A definite but less marked improvement was noted in the left side of the chest.

The endotracheal tube was strapped in position and she was nursed in an incubator with the head elevated. The oxygen was humidified by alevaire.

February 7, 1958.

1 a.m. Moist sounds were evident in all lung fields and 1 ml of thick pus was aspirated from the endotracheal tube.

3 a.m. 3–4 ml of thick yellow pus were aspirated from the endotracheal tube. The respiratory rate fell to 34 per minute and the colour became pink.

8 a.m. She became dyspnoeic and a further 1 ml of pus was aspirated from the endotracheal tube with some improvement.

10 a.m. Baby collapsed, became apnoeic and the heart rate slowed to 24 per minute. It was impossible to inflate the lungs by positive pressure. The endotracheal tube was removed and found to be completely blocked by inspissated secretions. Another tube was immediately inserted, secretions aspirated and the lungs reinflated by positive pressure with restoration of air entry to both lungs. Widespread crepitations were audible.

1 p.m. 1 ml of streptokinase (100 units) was introduced into the endotracheal tube and left for half an hour. Aspiration of a quantity of pus was associated with improvement in colour and activity.

Aspiration of smaller quantities of secretions was performed every 1–2 hours according to their presence in the endotracheal tube. Streptokinase was introduced 3-hourly.

11 p.m. Respirations were regular at 36 per minute, the air entry was good but widespread crepitations were present. The colour was satisfactory and the endotracheal tube was removed. The systolic murmur was barely discernible.

The pharynx was sucked out hourly and care taken to remove all secretions, an adequate exposure being obtained by placing a spatula in the baby's mouth and depressing the tongue.

February 8, 1958.

Moist sounds were audible at both bases. The respiratory rate had risen to 50 per minute. She was intubated and 1 ml of pus was removed. One hour later, the respiratory rate had fallen to 40 per minute. She took her feeds well and started to cry.

February 9, 1958.

She developed cyanosis, oedema of the sacrum, hepatomegaly and splenomegaly. The crepitations were more obvious on auscultation.

Intubation later on in the day resulted in the aspiration of 1 ml of whitish secretions.

February 10, 1958.

The hepatomegaly had decreased and oedema of the sacrum and the cyanosis had disappeared.

Intubation produced several plugs of yellow secretions. A considerable quantity of nasal secretions was also aspirated.

During the next 3 days the general condition and air entry improved. She was intubated daily and smaller amounts of secretions removed.

February 16, 1958.

The chest was clinically clear. She remained in hospital for a period of 2 weeks because of social conditions.

Comments. This baby was moribund on admission with secretions pouring from the pharynx.

(1) A phenomenal quantity of purulent secretions was aspirated during the first 24 hours. Even though the initial suction produced considerable aeration of both lungs, it was necessary to repeat the aspiration at frequent intervals in order to maintain this improvement.

(2) At one stage of the treatment blockage of the endotracheal tube with inspissated secretions resulted in collapse, bradycardia, apnoea and cyanosis. Fortunately the airway was quickly restored.

To avoid this complication, it was our policy to change the tube every 12 hours even if it appeared to be patent. We now consider, however, that the presence of abundant tenacious secretions warrants a change of endotracheal tube every 6 hours. Another reason for changing the tube periodically is that its junction with the metal endotracheal connection is often soaked in saliva. This tends to make the union less secure and the two may come apart.

(3) It is essential to have a sterile endotracheal tube ready for insertion in an emergency.

(4) In view of the fact that the larynx was very inflamed on admission, it may be considered that intubation would necessitate a tracheotomy. The baby was intubated seven times in all and in the initial stage the endotracheal tube was left in position for 24 hours. In spite of this treatment there was no evidence of any laryngeal stridor.

Case No. 11.

Repeated Intubation, Prolonged Intubation, Controlled Respiration, Tracheotomy

A male child aged 1 month, birth weight 5 lb. 6 oz. (2.5 kg), was admitted with a history of reluctance to feed, "snuffles" and cyanotic attacks.

On examination he was cyanosed, deeply uncon-

scious, with atony of all limbs. His colour improved in oxygen but respiratory distress remained severe, with marked rib recession and long periods of apnoea.

The percussion note was dull over both lung fields Breath sounds were absent over the whole left lung and crepitations and expiratory rhonchi were marked on the right side.

The larynx, when visualized, was found to show marked inflammation and a thin stream of pus trickled through the rima glottidis. The child was intubated, without relaxant, and a large quantity of fluid secretions removed by suction, aided by posture and percussion of the chest.

Following this procedure the air entry was greatly improved in all areas, the mucous membranes were pink and the child was coughing actively. The endotracheal tube was removed and the airway at this stage appeared satisfactory.

Improvement was maintained during the next 2 days. Feeding by tube was accomplished and the airway maintained by nasal and pharyngeal suction with posture and percussion of the chest.

Thereafter the condition again became critical, with cyanosis, rib recession and little air entry into the left lung. During this period he required repeated intubation and suction. The laryngeal oedema became so severe as to cause respiratory obstruction.

In view of this and the fact that periods of apnoea were frequent, the endotracheal tube was retained for some hours and respiration controlled. Tracheotomy was later performed as an elective procedure in theatre.

During the next week the child improved. Suction was maintained through the tracheotomy tube, on each occasion being followed by reinflation of the lungs through a cut-down Magill tube inserted into the tracheotomy tube. Periods of restlessness responded well to small doses of pethidine by intramuscular injection.

After 10 days the larynx being reasonably healthy, it was possible to remove the tracheotomy tube. Progress thereafter was satisfactory and the child was discharged home 26 days after admission.

Comments. (1) Where mechanical obstruction of such degree exists, there would appear to be no alternative to intubation and suction, whether the larynx be oedematous or not.

(2) In conjunction with modern antibiotics, tracheotomy gave rise to no difficulties other than those associated with the small size of the infant's air passages.

Case No. 8.

Tracheotomy

A female child aged 24 months, was admitted suffering from respiratory distress and cyanosis.

September 26, 1957.

On examination she was extremely ill, cyanosed and restless. The breathing was shallow and irregular. Marked rib recession was accompanied by action of all her accessory muscles of respiration. She was unable to cry.

Auscultation showed diminished air entry throughout the chest, which was due to laryngeal oedema. There were no adventitious sounds in the lungs, but secretions were audible within the trachea.

A tracheotomy was performed, and thick yellow pus was aspirated from the trachea. Restoration of the airway was accompanied by the disappearance of all the signs associated with respiratory embarrassment.

She was nursed in an oxygen tent with alevaire, the secretions were aspirated and the position changed periodically. She progressed satisfactorily.

September 29, 1957.

The mucus became more tenacious and within a few hours she gradually developed her original signs of respiratory embarrassment. Radiography showed collapse of the right middle and left lower lobes.

Bronchoscopy through the tracheostome under general anaesthesia showed the presence of a considerable quantity of sticky, blood-stained secretions. These were removed and the airway restored with considerable clinical improvement.

September 30, 1957.

She again deteriorated. The airway appeared clear, but on auscultation there was absence of air entry in the left side of the chest. Bronchoscopy revealed the presence of hard, inspissated and blood-stained material which was removed by forceps and suction. Her condition improved and radiography showed that the left lower lobe had expanded but there was "shadowing in the right upper and middle zones".

15 hours later. The above picture was again repeated and bronchoscopy enabled further removal of tracheal casts.

October 1, 1957.

A similar episode necessitated bronchoscopy with toilet to the bronchial tree. Her clinical picture, however, did not improve as well as previously. Respiration remained somewhat laboured and the child appeared to be exhausted.

3 hours later. Her dyspnoea increased and it was considered unlikely that she had had time to form further tracheal casts. 5 ml (100 units) of streptokinase were injected through the tracheostome and three hard inspissated clots followed by a fair amount of thin yellow pus were aspirated with considerable improvement in her condition. Streptokinase was injected 3 times a day for a period of 3 days.

In view of her desire to cough spontaneously during the above period of treatment it was decided to modify the standard tracheotomy tube. An Alder Hey tracheotomy tube (figs. 3, 4) was inserted which enabled her to cough effectively. The secretions coughed into the larger bronchi were then removed (Wilson, 1958).

October 11, 1957.

She gradually improved and the occluder was inserted into the tracheotomy tube.

October 22, 1957.

The tracheotomy tube was removed.

October 30, 1957.

She was discharged.

FIG. 3

The Alder Hey Tracheotomy Tube.

The inner tube has been removed and the occluder inserted, thus restoring the normal anatomical airway.

FIG. 4

The Alder Hey Tracheotomy Tube.

The inner tube is in place. Its expanded end provides for the attachment of the T-piece circuit and thus facilitates the use of positive pressure.

Comments. (1) It is essential to humidify the inspired air of patients subjected to tracheotomy, especially if secretions are abundant. In this case we had no humidifier, the inspired air being bubbled through water. It was feared from the start of treatment that tracheal casts would be produced and our suspicions were soon found to be correct.

It is probable that many of these complications would have been avoided if humidification had been satisfactory.

(2) This child had attempted to cough throughout the disease, but was unable to clear the bronchi of secretions.

The smaller divisions of the bronchial tree may be cleared effectively by one method only. The secretions must be coughed up into the larger bronchi. Patients with tracheotomies, however, are unable to cough effectively because they are unable to build up the requisite intrathoracic pressure, as the larynx is partly deprived of its natural function. In the adult, if the patient is conscious, this disadvantage may be obviated by asking him to inspire, when coughing may be made effective by occlusion of the tracheostome. Smaller children and especially infants usually will not co-operate in this manner. Even if they do, the respiratory rate is much higher and it is difficult to correlate occlusion of the tracheostome with the inspiratory and explosive efforts of the child. Occlusion of the tracheostome at the wrong time will cause distress due to the resultant feeling of suffocation. Also, the increased negative pressure arising in the alveoli may cause further alveolar collapse.

It was with the above factors in mind that it was decided to modify the tracheotomy tubes in present use (figs. 3, 4). The occluder, when inserted, restores the normal anatomical airway. If the child is trying to cough either spontaneously or after stimulation by catheter the inner tube may quickly be removed and the occluder inserted. The normal airway being thus restored, coughing will be instantly effective, provided the laryngeal orifice is not completely occluded. Any sputum produced may then be expectorated through the normal channels or collected from the larger bronchi by means of a catheter, on removal of the occluder.

This method, therefore, has the advantage of restoring the normal anatomical airway which may again be converted into a tracheotomy in a few seconds.

DEATHS

Of the eighteen cases presented in table I there were five deaths (cases 1–5).

(1) A malnourished premature infant, whose circulation failed to respond when adequate aeration of the lungs was re-established. The child remained pale, apnoeic and hypothermic in spite of controlled ventilation and good air entry into all areas. She eventually died from circulatory failure after efforts to correct this had proved unsuccessful. It is probable that she had been subjected to prolonged hypoxia.

Postmortem examination revealed scattered areas of consolidation in both lungs, free fluid in the pleural and peritoneal cavities and a patent ductus arteriosus.

(2) This child responded well to intubation and suction on two occasions. During the night he became totally obstructed, due either to inhalation of vomit or massive accumulation of secretions, and died of asphyxia before expert attention was available. Intubation was performed and inflation of the lungs found to be impossible prior to the removal of obstruction material by suction.

(3) This case has already been described and attention drawn to the fact that, despite grave cardiac lesions, death was primarily due to mechanical obstruction of the airway.

(4) A premature infant whose respiratory distress was due to bronchiolitis. He responded well to intubation and controlled respiration. After being intubated nine times, and for several prolonged periods, laryngeal oedema became so severe as to necessitate tracheotomy. His postoperative condition was very satisfactory.

During the night he became cyanosed, failed to respond to inflation of oxygen through the tracheotomy tube and rapidly died. Unfortunately we were not present and were unable to assess the state of the airway as the tracheotomy tube was removed soon after death. The history obtained from those in attendance suggests that the tracheotomy tube had become dislodged and was no longer in the trachea.

Autopsy showed patchy collapse of both lower lobes, with scattered areas of inflammation. There was some degree of cerebral oedema.

(5) A twin, this child was the elder brother of case no. 6. He was admitted one day later and followed the same downhill course, until, collapsed, cyanosed and with totally inadequate tidal ventilation and poor air entry in all areas of both lungs, he required intubation and suction.

He responded well. The mucous membranes became pink, and he coughed on the tube. Respirations remained periodic in character, however, and it was considered wise to retain the tube in position and control respiration when required.

The tube was changed at frequent intervals and suction applied as required. Unfortunately, again at a period when we were unable to provide instant attention, the tube became blocked by secretions and the child died from asphyxia before they could be removed.

Of these five deaths, at least three are primarily due to respiratory obstruction. It is to be hoped that, when these cases are concentrated in a single unit where expert attention is instantly available at all times, such deaths will prove to be avoidable.

DANGERS AND COMPLICATIONS

That many difficulties may be encountered in the management of these cases may be clear from the case histories above. Constant detailed supervision is essential to avoid and overcome the many possible complications.

The greatest danger, even with an endotracheal tube in place, still comes from respiratory obstruction, due to the accumulation of secretions or blockage of the tube from various causes.

Laryngeal Oedema.

It is held in some quarters that intubation of the infant's larynx frequently results in oedema which may require tracheotomy for relief. During the past five years 35,000 children of all ages have been intubated for surgical purposes at Alder Hey and Royal Liverpool Children's Hospitals. This number has included many hundreds of infants. No such case has yet required tracheotomy as a result of laryngeal trauma.

Where respiratory infection exists, however, laryngeal oedema must be accounted more likely. Case no. 11 already had marked laryngeal oedema before intubation, which undoubtedly aggravated the condition and necessitated tracheotomy. Case no. 4 similarly had a moderate degree of laryngeal oedema prior to intubation and tracheotomy was required after the procedure had been repeated nine times. It may be thought inevitable that a certain proportion of cases will require tracheotomy where such methods of treatment are essential to overcome respiratory obstruction.

In these cases without marked primary oedema, however, repeated and prolonged intubation have resulted in remarkably little damage to the larynx. Several additional cases of neonatal respiratory distress, not primarily of an infective nature, have been treated with endotracheal tubes in position for several days without harmful results to the

larynx. In one remarkable case of neonatal tetanus, Rees and his colleagues retained an endotracheal tube in position for 34 days and performed bronchoscopy twice daily without marked laryngeal oedema.

With these facts in view, we consider that the advantages offered by intubation by far outweigh the possible disadvantage of laryngeal oedema.

Bronchopleural Fistula.

Spontaneous rupture of a lung abscess may occur into a bronchus or into the pleural cavity, or both. If the bronchial tree is flooded by secretions, intubation and suction may be required to prevent asphyxia. That the use of positive pressure may produce a pneumothorax in these cases is well shown in case no. 3.

It follows that such a possibility must be constantly kept in mind, especially where the infecting organism is the staph. pyogenes, and careful watch maintained on the response of the lungs and mediastinum to positive pressure.

Where such a condition is known to exist and intubation and suction are indicated, it is wise to refrain from using positive pressure until preparations for pleural drainage are complete.

SUMMARY

In spite of modern advances in treatment, there is still a significant rate of mortality in infants who suffer from acute respiratory infections.

Failure to clear secretions from the air passages results in severe respiratory obstruction and increasing hypoxia. Oxygen demand is increased by virtue of the increased respiratory effort, while oxygen supply is diminished because of the defective ventilation.

When such a state of respiratory insufficiency exists, antibiotics are of little value unless the airway can be maintained until such time as they can exert their beneficial effect. Similarly, an obstructed airway must reduce the value of oxygen therapy.

Methods by which this state of respiratory insufficiency may be alleviated are discussed. These include the use of endotracheal intubation, suction, bronchoscopy, tracheotomy, posture and humidity; and of controlled respiration where the infant is too weak to maintain adequate ventilation by its own unaided efforts.

A series of eighteen cases treated by such methods is described. Thirteen of these infants survived. Several case histories are presented in some detail while others are included in tabular form.

The five deaths which occurred in this series are discussed. In certain of these cases the presence of associated lesions rendered survival unlikely.

Some complications which may arise are mentioned, in particular those arising from endotracheal intubation in infants. While these problems exist, they should not be held to contraindicate this procedure, especially in cases where intubation and suction are essential for relief of respiratory obstruction and the re-establishment of adequate ventilation.

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CORRESPONDENCE

HALOTHANE AND THE ROWBOTHAM'S BOTTLE

Sir,—A few weeks before publication of my paper "Halothane concentration from a Rowbotham's bottle in a circle absorption system" (*Brit. J. Anaesth.* (1958), **30**, 312) there appeared on the market a modified Rowbotham's bottle produced by the British Oxygen Company; this version is wickless and has downward facing ports and a larger liquid container. The company claims that it delivers trichloroethylene vapour in similar concentrations to the old pattern (B.O.C. and M. & I. E. makes); this may or may not be so, but when used in a circle absorber with halothane I find that concentrations in excess of the figures stated in my paper are obtainable. Actual readings cannot at the present time be given until further more accurate estimations have been made; however, as a rough and safe clinical guide, half to three-quarters "ON" with the new bottle is equivalent to "FULL ON" in the old, for vaporization of the first 10–15 ml of halothane, i.e. for the first hour.

A new vaporizer, offering minimal resistance to respiration, has been designed and is in the process of manufacture, testing and calibration, but this will not be available for purchase for some months, meanwhile it seems advisable to warn would-be users of the newly introduced B.O.C.'s Rowbotham's bottle of the possibility of now producing concentrations of halothane in a circle system in excess of 3.5 per cent.

It was reassuring to see confirmatory clinical evidence by Brown and Woods (*Brit. J. Anaesth.* (1958), **30**, 333 and 338) for a lack in build-up of concentration of halothane with a circle absorber but I feel it is a pity that they should advocate disembowelling and relining an otherwise satisfactory piece of apparatus when they already possess an adequate alternative.

P. J. C. BURTON
Southlands Hospital,
Shoreham-by-Sea

ERRATUM

The following correction should be made to the paper on "Halothane concentration from a Rowbotham's bottle in a circle absorption system" by P. J. C. Burton in the July 1958 issue (*Brit. J. Anaesth.*, **30**, 312):

Page 312, column 2, line 21, should read:

". . . Atropine 0.6 mg"

Brit. J. Anaesth. (1958), **30**, 435

THE ROLE OF HALOTHANE IN THE PREVENTION OF SURGICAL SHOCK*

BY

MICHAEL JOHNSTONE

Department of Anaesthetics, Royal Infirmary, Manchester, England

THE PATHOGENESIS OF "SHOCK"

The study of shock has occupied the minds of medical men for over two centuries and the documentation has reached relatively enormous proportions. Several excellent reviews of the literature have been published (Nelson, 1957; Millican and Rosenthal, 1954; Frank, 1953; Drew, 1942). These reviews indicate that most of the work to date has been done by surgeons, physicians, and physiologists who have proved conclusively that the maintenance of the blood volume is the most important single factor in the prevention and treatment of shock. Clarke (1957) suggested that the failure of response to blood transfusion was due mainly to too little blood too late. The rapid intravenous infusion of large amounts of blood has been shown to cause acute right-sided heart failure secondary to the intense vasoconstriction of the pulmonary arterioles caused by the citrate used to prevent coagulation of the stored blood, a reaction which can be prevented by the intravenous administration of calcium gluconate and procaine hydrochloride (Firt and Hejhal, 1957).

Opinions differ as to the best method of replacing blood lost in severe haemorrhagic shock; some recommend the intravenous route, others the intra-arterial, and others the intra-aortic. A fourth revolutionary method consists essentially in rapid intravenous infusions after the administration of vasodilator substances (Martin, 1955). Whilst the transfusion approach to the shock problem is perfectly logical in cases where blood loss is obvious, it must be admitted that shocked patients are not infrequently encountered in whom transfusion by conventional methods appears to be not only useless but detrimental because of the risk of pulmonary oedema. In many instances the delay associated with the restoration of the blood volume must inevitably have deleterious effects on the patient, e.g. strangulated hernia, gastric perforation and peritonitis, intestinal volvulus, mesenteric embolism, etc. It is with this latter group that my interest lies, because I am convinced that the solution to the problem is in the hands of the pharmacologist and his clinical counterpart, the anaesthetist.

There is much confusion as to the meaning of the term "shock", many different definitions having been provided. I feel that the misunderstanding derives mainly from the fact that too much attention has been paid to the finer aetiological factors, in the sense that it appears to have been assumed that different agents cause a fundamentally different type of shock syndrome—thus we have traumatic shock, haemorrhagic shock, surgical shock, obstetric shock, endotoxic shock, anaphylactic shock, histamine shock, vasovagal shock, cardiac shock, neurogenic shock, anaesthetic shock, and adrenaline shock. This picture has been further complicated by the presentation of clinical symptomatologies in which there has been little effort to differentiate between the signs of impending shock and those of established shock.

In view of this rather bewildering state of affairs I have endeavoured to simplify the issue by starting at the wrong end, that is, to concentrate on established cardiovascular collapse and to describe it as something analogous to a fugue in three parts: the exposition, the response, and the counterpoint; the exposition being the stimulus or injury which provokes the shock response of the cardiovascular system; the counterpoint being the means we adopt to counteract both the initiating stimuli and the cardiovascular reaction. In the management of shocked patients, as in the fugue form of music, there is a constant inter-

* A paper read before the Section of Anaesthetics of the Manchester Medical Society on April 24, 1958.

weaving of these three elements which renders almost impossible the study of each as a separate clinical entity.

Figure 1 illustrates diagrammatically the cardiovascular picture of a normal man. This subject has a normal blood volume, his skin is warm and pink and the veins are visible. Circulation is at optimal efficiency in the liver, kidneys, intestines, lungs, heart, and brain. Circulatory homeostasis is maintained by the neuro-endocrine system from control centres in the hypothalamic and medullary regions. Functional integration of the neuro-endocrine and cardiovascular systems permits the circulation to adapt immediately to environmental changes and directs adequate blood supplies to the tissues with priority demands. Under conditions of acute stress, such as trauma or certain forms of anaesthesia, the neurogenic vasomotor stimuli are mediated by the chemical transmitters adrenaline and noradrenaline.

For some reason our subject suffers a profound shock and figure 2 illustrates diagrammatically the dismal state of his circulation. He may have sustained a severe crush injury or his stomach may have perforated; he may have had a coronary occlusion or a volvulus of his intestines; there may have been a sudden haemorrhage or he may have been given an overdose of adrenaline; he may have been subjected to a severe emotional crisis, or he may have undergone prolonged and deep anaesthesia with a toxic agent. The ultimate cardiovascular state is one of intense peripheral vasoconstriction, the common denominator in virtually all forms of shock irrespective of the cause. The skin becomes cold, clammy, pale, and cyanotic; the pulse is rapid, thin, and feeble, and the veins disappear; the intestines, kidneys and liver become pale and bloodless, the spleen contracts, and the rate and force of the cardiac contractions increase. This vasoconstrictive reaction is primarily protective in nature, being designed to restrict blood and fluid loss and to maintain the blood supply to the brain and myocardium. It also constitutes an effective barrier to the rapid restoration of the blood volume by either the venous or arterial routes.

During the past few years an accumulation of evidence has indicated that the development of the so-called irreversible stage of shock may well be due to excessive prolongation of the vaso-constrictive reaction which, after a time, becomes self-perpetuating (Paton, 1957; Boba and Converse, 1957; Zweifach and Thomas, 1957; Martin, 1955). In the earlier stages of shock the constrictor actions of circulating adrenaline and noradrenaline are intensified by a vasoexcitor material (V.E.M.) released from the ischaemic kidneys. As the shock state persists the sensitivity of the peripheral vessels to adrenaline and noradrenaline is abolished by the vasodepressor material (V.D.M.) released by the ischaemic liver (Nelson, 1957), causing pooling and stagnation of blood in the peripheral vessels, presumably the irreversible stage—hyporeactivity and stasis with "back-flow" in the terminal vascular bed. There is reason to believe that intravascular clotting occurs at this stage, leading to the formation of multiple minute pulmonary emboli which enhance the asphyxial state of the patient and ultimately lead to his death (Crowell and Read, 1955; Adelman and Katz, 1957). Survival after prolonged or severe vasoconstriction is not infrequently followed by death from uraemia—the so-called "crush syndrome" or lower nephron nephrotic syndrome—or by death from hepatic failure in patients with established liver disease (Shackman et al., 1952, 1953; Himsworth, 1950).

The activity of the vasomotor section of the sympathetic system is largely responsible for initiating this unhappy train of events. As with all neuronal circuits the vasomotor system consists of a central station, situated in the floor of the fourth ventricle, which receives afferent signals from several peripheral receptor areas and dispatches them along the efferent pathways to the heart, blood vessels, and viscera. The afferent stimuli originate in receptors of four different types, namely, the baroreceptors, the chemoreceptors, sensory or pain receptors, and cerebral cortical influences (fig. 3).

Baroreceptors.

These are located in the carotid sinus and aortic arch and are activated by changes in blood pressure from any cause, e.g. hypovolaemia, myocardial damage, or postural pooling of blood.

Chemoreceptors.

These are situated in the carotid and aortic bodies and are stimulated by carbon dioxide and changes in the pH of the blood. Oxygen defi-

FIG. 1

BACTERIAL TOXINS
EMBOLISM
TOXIC METABOLITES
GLYCOGENOLYSIS
POTASSIUM LOSS
HEPATIC FAILURE
URAEMIA
'CRUSH' SYNDROME

FIG. 2

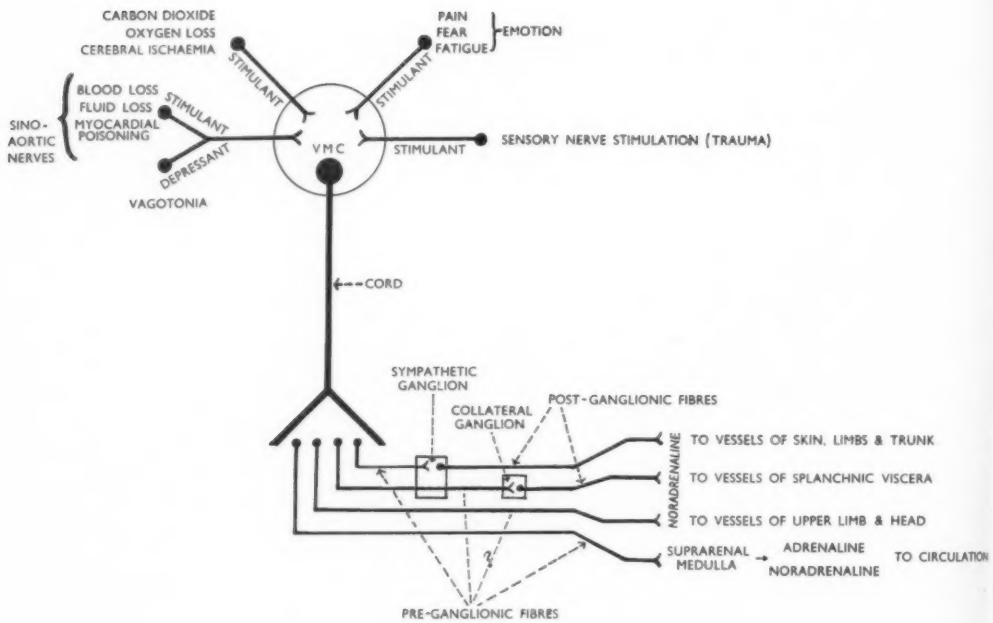

FIG. 3

Diagram of the vasomotor centre with its afferent and efferent connections.

ciency also exerts a stimulant effect on them. Probably the best example of shock due mainly to activation of these receptors is the profound collapse which sometimes follows gastric perforation in elderly males with fixation of the costo-vertebral joints: diaphragmatic rigidity secondary to peritonitis seriously restricts respiration causing partial asphyxia and shock which often responds dramatically to the restoration of normal tidal volumes. Chemoreceptor activity is also present in the shock which follows acute coronary occlusion and is also suspected to be present to some degree in the intense vasoconstriction due to B. Coli endotoxin liberated from ischaemic bowel in such conditions as mesenteric embolism, intestinal volvulus, and strangulated hernia. Carbon dioxide retention is a well-known cause of circulatory collapse during or following general anaesthesia.

Sensory Afferents.

It is well recognized that severe pain can cause profound shock. This has been confirmed experimentally by stimulation of sensory nerves in experimental animals. Shock from this cause is sometimes observed clinically when patients emerge quickly from anaesthesia after trivial operations such as haemorrhoidectomy, and is easily avoided by the timely administration of an analgesic. General anaesthesia, particularly the very light planes of the nitrous oxide-curare technique, does not always adequately protect the patient from this type of vasomotor activation. Drenching sweats, with pallor and vasoconstriction, are commonly encountered during abdominal surgery in inadequately anaesthetized patients (Loder, 1957). Some of the most severe degrees of shock I have seen occurred in patients undergoing prolonged neurosurgical operations under local analgesia.

Cortical Afferents.

The influence of the emotions on vasomotor activity is well known (Gellhorn, 1943). Anxiety states have been shown to cause peripheral vasoconstriction (Ackner, 1956) and the intimate relation between emotional disturbances and essential hypertension has recently been described (Boshes, 1958). The anaesthetist not uncommonly encounters quite severe degrees of vasoconstriction, sometimes with hypotension, in non-premedicated patients in the immediate pre-operative phase. Similarly, minor surgery performed under local analgesia, is sometimes associated with severe circulatory collapse in the absence of blood loss. In these circumstances the induction of sleep promptly causes a striking improvement in the peripheral circulation.

Efferent Pathways of the Vasomotor System.

Fibres arise in the centre and pass down the cervical cord to end in the sympathetic cells of the lateral grey horns of the thoracic and upper lumbar segments of the cord. The preganglionic fibres then leave the cord via the anterior roots and pass peripherally in four different types of relay system (fig. 3):

(1) Most of them form synapses in the paravertebral ganglia of the sympathetic trunk and pass thence as postganglionic fibres to the peripheral vessels and viscera.

(2) Some pass uninterruptedly through the paravertebral ganglia and emerge as sympathetic nerves, passing to synapses in the collateral ganglia, e.g. the splanchnic nerves and the mesenteric ganglia. Postganglionic fibres emerge from the collateral ganglia.

(3) Some fibres run to the peripheral vessels with no connections with the paravertebral or collateral ganglia. These arise from the sympathetic cells of the upper dorsal and upper lumbar segments of the cord (Alexander et al., 1949).

(4) The sympathetic nerves to the suprarenal medulla are preganglionic all the way, the cells of the suprarenal medulla being regarded as postganglionic sympathetic cells resistant to the action of ganglionic blockers (Hollinshead, 1936; Hall, 1957).

In addition to these central and peripheral sympathetic connections there also exists the phenomenon known as the "peripheral autonomy" of the sympathetic system (Rothlin and Berde, 1949–53) by means of which circulatory homeostasis can be maintained after destruction or inactivation of the peripheral connections of the vasomotor system. This phenomenon is associated with the development of hypersensitivity to the vasoconstrictor effects of adrenaline and noradrenaline (Gellhorn, 1943). All these factors and variations have to be taken into account when

assessing the activity of a ganglionic blocking drug or technique.

TO WHAT EXTENT IS ANAESTHESIA INVOLVED IN THE PATHOGENESIS OR IN THE PREVENTION OF SHOCK?

Those who have been in practice long enough will have little difficulty in recalling the profound circulatory collapse which not infrequently followed prolonged and deep anaesthesia with chloroform, ether, cyclopropane, or thiopentone. It has been repeatedly demonstrated that these agents have a depressant effect on the myocardium which is more than adequately compensated by an increased production of adrenaline and noradrenaline brought about by sympathetic stimulation (Watts, 1955; Brewster et al., 1953). Prolonged sympathetic stimulation ultimately causes intense peripheral vasoconstriction with hypotension, tachycardia, and sweating (Freeman, 1933; Paton, 1957), with delayed recovery of consciousness due to the difficulties of excretion of the anaesthetic agent created by the impaired circulation. The afferent stimuli which provoke the vasoconstrictor reaction probably arise in the baroreceptors secondary to the myocardial weakening, but there is also the possibility of direct stimulation of the vasomotor centre (McAllister and Root, 1942). Chemoreceptor activity may also be involved as some degree of asphyxia must have been the inevitable consequence of prolonged and deep anaesthesia, most of these agents being highly irritant to the air passages, causing excessive secretions and bronchiolar constriction not always amenable to the effects of atropine. In the surgical management of shocked patients it is illogical to use anaesthetic agents which of themselves are capable of inducing shock.

Spinal Anaesthesia.

The introduction of spinal anaesthesia was the first attempt to control the peripheral circulation by blocking the vasomotor efferents. Labat (1931) observed that patients with crush injuries of the lower extremities were improved by spinal anaesthesia provided a head-down position was maintained and vasopressors were not used. This approach was extended by Griffiths and Gillies (1948) with their "total spinal" technique and recently epidural block has been used successfully in the treatment of severe refractory shock due to coronary occlusion (Agress, 1958). Loder (1957) has called attention to the effectiveness of blocking the collateral sympathetic ganglia in the prevention of shock during elective abdominal surgery. The spinal block proved to be of limited use because it did not influence, or perhaps even intensified, the emotional and asphyxial factors, as well as having other technical disadvantages. It should be noted, however, that it is still the only method of sympathetic block which completely isolates the vasomotor centre from the periphery.

Muscle Relaxants.

The arrival of the muscle relaxants was a major step in the elimination of shock from elective surgery, due mainly to the fact that they abolished the need for the toxic inhalational agents (Harroun et al., 1946; Gray and Halton, 1946; Cullen, 1944). It is doubtful whether the relaxants have any direct effect on vasomotor function because they have not by any means completely eliminated the incidence of shock during elective surgery (Loder, 1957). The asphyxial basis of vasomotor overactivity has, if anything, been intensified by some of the relaxants because the need for positive pressure inflation of the lungs has, in certain circumstances, disastrous effects on the normally low impedance of the pulmonary circulation (Maloney et al., 1951; Johnstone, 1956). All accepted methods of controlled respiration are but the crudest substitutes for the beautifully integrated movements of blood and gas so constantly effected by spontaneous respiration (cf. Rodbard, 1953).

Ganglion blocking drugs.

Then came the ganglionic blockers. Although primarily designed to limit bleeding during operations (Rollason, 1953) it soon became apparent that these agents afforded some protection against the development of shock during elective surgery. Attention immediately became focussed on the possibility that vasomotor overactivity was probably the essential cause of peripheral circulatory failure and several important papers supporting this concept have now been published (Martin, 1955; Boba and Converse, 1957; Paton, 1957). The ganglionic blockers hexamethonium and trimetaphan act mainly on the parasympathetic

synapses and on the synapses of the paravertebral and collateral sympathetic ganglia and do not appear to exert any significant effect on the synapses within the suprarenal medulla (Hall, 1957; Kurnick, 1956; Moe and Freyburger, 1950: Freyburger et al., 1948). The sympathetic connections between the periphery and the sympathetic cells of the upper dorsal and upper lumbar segments may be uninfluenced by ganglionic blockers because not only does ganglionic blockade fail to block the hypertensive response to carbon dioxide (Payne, 1958) but bilateral adrenalectomy also fails to do so (Von Euler and Franksson, 1957; Johnstone, 1958); the rise in blood pressure under the latter circumstances is presumably due to the release of noradrenaline by activation of the vasomotor system.

The blocking action of hexamethonium and of trimetaphan on the cardiac parasympathetic ganglia constitutes a major and perhaps dangerous obstacle to their safe use in clinical anaesthesia. The combination of hypotension due to sympathetic blockade with tachycardia due to parasympathetic blockade may have disastrous effects on the cardiac output, particularly in the presence of organic disease of the coronary arteries: the short diastolic times may prevent complete ventricular filling at low blood pressures. At best these agents produce only a partial block of the vasomotor efferents and have no effect on the afferent stimuli which will still be relayed to the cardiovascular system through the efferents unaffected by the blockade. There is no doubt, however, that they can be used effectively and beneficially during anaesthesia in patients without organic disease of the cardiovascular system, provided non-toxic narcotic agents are used, respiration controlled with extreme care and complete oxygenation and efficient elimination of carbon dioxide are ensured. Controlled respiration by intermittent positive pressure during ganglionic blockade should be regarded as hazardous because of the abolition of the vascular compensatory mechanisms which normally counteract the raised intra-alveolar gas pressures (Barer and Nusser, 1957; Hubay et al., 1954; Saklad, 1954; Finnerty and Freis, 1950).

Chlorpromazine.

Chlorpromazine (Laborit et al., 1952) was the next drug to be used for the control of shock and was used in an attempt to suppress both the afferent and efferent vasomotor stimuli. It effectively modifies the emotional and sensory afferents and induces a peripheral vasodilatation by blocking the vasoconstrictive actions of adrenaline, noradrenaline, and other vasopressors (Dripps et al., 1955). The antipressor action of chlorpromazine, and of the various other adrenolytic drugs, would appear to be a contra-indication to their use either before or during operative surgery. Patients under sympathetic blockade at any site are notoriously liable to disastrous degrees of hypotension following sudden haemorrhage or abrupt changes of posture. In these circumstances the unimpaired effectiveness of a peripherally acting vasopressor such as methoxamine can be life-saving. A further disadvantage of chlorpromazine is that it combines hypotension with tachycardia which, as with hexamethonium, may have serious effects on the cardiac output and coronary circulation.

Halothane.

Halothane is the latest anaesthetic to be used for the control of shock during elective and emergency surgery. It was discovered by Suckling (1957, 1958, 1958a) as the result of an investigation into the synthesis of nontoxic, nonexplosive, volatile anaesthetic compounds, a synthesis based on the physical and chemical principles described by Ferguson (1939, 1951). Subsequent pharmacological observations (Raventos, 1956; Raventos and Spinks, 1958; Spinks, 1958) gave every indication that it was the compound most likely to succeed in clinical practice. During the past few years extensive clinical trials have been reported (Bryce-Smith and O'Brien, 1956; Marrett, 1957; Brennan et al., 1957; Robson and Sheridan, 1957; Hudon et al., 1957; Robertshaw, 1957; Hartung, 1957; Reinhold et al., 1957). These reports indicate that an outstanding feature of halothane anaesthesia is the excellent condition in which it leaves the patient after major surgery under prolonged and deep anaesthesia. Pope (1957) has demonstrated that it may well be the anaesthetic of choice for surgery in elderly patients with advanced cardiovascular and pulmonary diseases, a group which has been particularly refractory to most other agents and techniques; his reason for this claim is that halothane, in addition to pro-

viding ideal operating conditions, appears to prevent shock and circulatory collapse.

I have now anaesthetized with halothane over 2,500 patients undergoing major surgical operations of all kinds and I have not seen any evidence of shock as manifested by tachycardia, sweating, pallor with vasoconstriction, impaired response to intravenous transfusion and to methoxamine, and delayed recovery of consciousness, even after severe accidental haemorrhage during the operations. In all cases vasodilatation with dry and warm peripheries and normal pulse rates have persisted throughout the period of anaesthesia. Profound hypotension may be encountered as the consequence of haemorrhage or of postural influences and is easily corrected by the appropriate treatment—transfusion, methoxamine, or both. Particularly good results have been obtained in patients shocked by intestinal catastrophes such as prolonged obstruction, mesenteric embolism, strangulated hernia, etc. These patients are almost invariably severely dehydrated and the intense vasoconstriction is a major obstacle to the restoration of blood volume, tissue hydration, and oxygenation. It these cases anaesthesia is induced and maintained with halothane with either oxygen or nitrous oxide-oxygen mixtures. As soon as venous dilatation appears—two to three minutes—fluids can be very rapidly administered intravenously till the blood pressure reaches reasonable levels. There has been no evidence of pulmonary oedema from the rapid infusion of fluids, presumably because the dilated state of all the blood vessels facilitates the rapid distribution of the fluid throughout the tissues of the body—needless to say, a head-down tilt should be maintained until the blood volume is deemed to be restored. With this technique, patients can be resuscitated whilst the surgeon operates and valuable time gained, and it is hoped that this will be the answer to many of the problems associated with emergency surgery in shocked patients.

There has been much controversy concerning the cause of the vascular hypotension induced by halothane. Raventos (1956) indicated that it was due mainly to sympathetic blockade, particularly of the mesenteric ganglia, and he demonstrated a selective affinity for certain ganglia. The failure of Burn et al. (1957) to find much evidence of complete blockade in the superior cervical ganglion of the cat does not exclude a block of other ganglia. Paton (1952) has stated that the superior cervical ganglion of the cat can be very resistant to blockade and selectivity is a feature of all ganglionic blockers, the response of different ganglia to different blockers being considerably influenced by the "background tone" and by individual variations in sensitivity.

The suggestion that the hypotensive effect of halothane is due mainly to myocardial weakening (Burn et al., 1957) is incompatible with the persistence of the sensitivity of the peripheral circulation to the hypertensive action of methoxamine (Brewster et al., 1953) and of carbon dioxide; nor is it consistent with the rapid and persistent rise in blood pressure which follows intravenous transfusions during halothane anaesthesia. It has been conclusively demonstrated that a hypotension due to myocardial depression is uninfluenced by methoxamine (Brewster et al., 1953).

The isolated heart-lung preparation (Burn et al., 1957) has revealed a distinct myocardial depression with halothane; this observation is not strictly relevant to and is of little help in explaining the effects of halothane in clinical practice, the heart-lung preparation being in no way comparable to the intact cardiovascular system with its intricate compensatory mechanisms. It should not be forgotten that surgical concentrations of ether, widely regarded as a "safe" anaesthetic, have a deleterious effect on the heart-lung preparation (Brewster et al., 1953) whereas in the intact animal the cardiac output is increased (Blalock, 1927). The rather complex clinical experiments of Severinghaus and Cullen (1958) from which it was deduced that the halothane hypotension was due to myocardial depression, are difficult to interpret owing to the fact that unspecified concentrations of the drug were administered by the artificial inflation of the lungs of patients paralysed with suxamethonium, a manoeuvre which, quite apart from halothane, has been shown to have serious effects on the cardiac output (Johnstone, 1956). One of the outstanding advantages of halothane anaesthesia is that major surgery, including abdominal but excluding thoracic, can be performed for the most part whilst the patient breathes spontaneously. It is not improbable that spontaneous respiration does much to maintain the efficiency of the pulmonary circu-

lation and the venous return to the heart, particularly in the presence of hypotension with sympathetic paresis. Halothane combined with controlled respiration either by relaxants or by central depressants can be used effectively for thoracic surgery, satisfactory results in large numbers of cases having been obtained by Hartung (1957) and by Robertshaw (1957). In using halothane with controlled respiration considerable care should be exercised in limiting the concentration of halothane vapour to the minimal surgical requirements.

The clinical picture of halothane anaesthesia has a striking resemblance to the picture of the "hexamethonium man" described by Paton and Zaimis (1952) and again by Paton (1957). The hypotension with the dry, warm, and pink skin with dilated veins; the suppression of salivary, bronchial, and gastric secretions; the tendency to postural hypotension and the pooling of blood in dependent parts; the absence of the usual sympathoadrenal response to trauma and haemorrhage; the atonic bowel; the persisting sensitivity of blood vessels to peripherally acting vasopressors; the sensitization to the autonomic transmitter substances, and the immediate response to intravenous transfusion. The disappearance of the shock syndrome as a result of halothane anaesthesia is in keeping with Paton's concept of a "controlled circulation" effected by sympathetic blockade at ganglionic level.

There is no doubt that halothane, in common with other anaesthetic agents, depresses the emotional and sensory afferents of the vasomotor system and, in addition, it inactivates the baroreceptors and leaves intact the chemoreceptor mechanism. The hypertensive response to carbon dioxide retention is unimpaired by halothane, and may even be exaggerated (Johnstone, 1958). Direct depression of the vasomotor centre by halothane, or by any other anaesthetic drug in clinical use, is almost certainly out of the question as the classic experiments of Hill and Macdonald (1933) revealed that this centre is amazingly resistant even to the direct application of such powerful protoplasmic poisons as procaine and cinchocaine.

The persistence of the hypertensive response to carbon dioxide retention during halothane anaesthesia indicates efficient conduction in the efferent sympathetic pathways within the spinal cord (Steck and Gellhorn, 1939). The hypertensive response to carbon dioxide retention does not occur in patients under halothane narcosis combined with high spinal anaesthesia. There is considerable evidence to indicate that the efferent sympathetic nerves to the suprarenal medulla are resistant to the effects of ganglionic blockers because stimulation of them by either direct methods or by carbon dioxide after the administration of ganglionic blockers, results in a rise of blood pressure due to the release of adrenaline and noradrenaline (Hall, 1957; Enderby, 1956). The hypertensive response to carbon dioxide retention during halothane anaesthesia in man cannot be regarded as being completely due to the release of adrenaline from the suprarenal medulla because it is still present after bilateral adrenalectomy (Johnstone, 1958). The rise in blood pressure is unlikely to be of cardiac origin as both systolic and diastolic pressures are equally involved suggesting that it is probably mediated by noradrenaline released at sympathetic nerve endings in some as yet unidentified part of the body, possibly the sympathetic connections of the upper dorsal and upper lumbar segments (Alexander et al., 1949).

In spite of the absence of clinical evidence to indicate a depressant effect on the heart it would be wise to assume, in the present state of our knowledge, that concentrations of halothane in excess of those required for surgical anaesthesia may have toxic effects on the myocardium. Reasonable care should therefore be exercised to ensure that the dose is limited to the surgical requirements of each patient. After two years of intensive clinical experience with halothane I see no reason to modify the previous statement to the effect that the occurrence of cardiac arrhythmias in the anaesthetized patient reflect more on the management of the patient than on the drugs used to induce and to maintain anaesthesia (Johnstone, 1955).

For the present it would seem reasonable to assume that halothane suppresses sympathetic activity at some level presumably ganglionic. As with all ganglionic blockers, the sensitivity of the ganglia to the blocking action varies from patient to patient and is selective in regard to the ganglia affected and to the degree in which they are

blocked. The cardiac parasympathetic ganglia appear to be completely spared by surgical concentrations of halothane because bradycardia, amenable to atropine, is invariably encountered during halothane anaesthesia; it is not known whether the slowing of the heart is due to activation of parasympathetic reflexes or to the abolition of the buffering action of the sympathetic system such as occurs in high spinal anaesthesia. This sparing of the cardiac parasympathetic ganglia is in one way a fortunate occurrence as it ensures ample diastolic times for complete ventricular filling at low systolic pressures.

Another reason for the excellent condition of patients during and after surgery under halothane-oxygen anaesthesia is that the development of hypoxia and anoxia is physically impossible in the presence of a clear airway, the oxygen uptake being almost completely independent of the tidal and minute respiratory volumes, being effected by the phenomenon known as apnoeic diffusion oxygenation (Holmdahl, 1956). During halothane-oxygen anaesthesia the oxygen uptake by diffusion is usually as efficient during apnoeic states as in normal respiration (Johnstone, 1958). The elimination of carbon dioxide is still dependent on the respiratory movements but this can be accomplished with ease because of the ideal state of the air passages—perfectly dry and relaxed with complete dilatation of the bronchioles in all patients including those with bronchiolar constriction due to pulmonary or cardiac disease. The ease with which patients ventilate during halothane anaesthesia is consistent with an autonomic blocking effect, Paton (1952) having postulated a similar action during autonomic blockade with hexamethonium. Several investigators have demonstrated the beneficial effects of sympathetic blockade on the respiratory functions of patients whose vital capacities were seriously diminished by cardiac and pulmonary disease (Bromage, 1956; Ellestead and Olsen, 1956). The importance of adequate oxygenation in the control of experimental shock has been described by Schnedorf and Orr (1941) who observed that oxygen inhalations caused a 70 per cent increase in the duration of life in dogs subjected to severe tramatic shock; similar observations were also made by Wood et al. (1940).

ILLUSTRATIVE CASE REPORTS

CASE 1. Male, 54 years. Severe haematemesis due to gastric ulceration. Heart and lungs normal. Blood pressure 70/50 mm Hg, pulse rate 125 beats a minute, sweating. Conservative treatment and blood transfusion restored the blood pressure to 110/70 mm Hg in 12 hours. Twenty-four hours later the patient collapsed again and immediate laparotomy was decided upon. Premedication, atropine 0.5 mg. On arrival at the operating theatre the blood pressure was 60 mm Hg systolic, the pulse rate 135 beats a minute, and the respiratory rate 35 a minute.

Anaesthesia was induced with nitrous oxide, oxygen and halothane and maintained with halothane and oxygen. During the first 20 minutes of anaesthesia the blood pressure was restored to 110/70 mm Hg by the rapid intravenous transfusion of 2 pints (1 l.) of blood and 1 pint (500 ml) of saline. The pulse rate dropped to 90 beats a minute, and the skin became warm and pink. A partial gastrectomy was then performed under halothane-oxygen anaesthesia with a total dose of 150 mg of suxamethonium to facilitate the initial exploration and subsequent closure of the peritoneal cavity. Throughout the operation which lasted 80 minutes, the blood pressure remained at 110 mm Hg systolic and the pulse rate gradually dropped to 80 beats a minute, a further pint of blood and 1 pint of saline being administered. Twenty minutes after the conclusion of the operation the patient recovered consciousness, the blood pressure being 120/80 mm Hg, and the pulse rate 90 beats a minute. The blood pressure did not fall subsequently and recovery was uneventful.

CASE 2. Male, 64 years. Gastric ulcer perforation of 12 hours duration. Chronic bronchitis with emphysema. Very collapsed, cyanosed, sweating, and dyspnoeic. Blood pressure 100/80 mm Hg, pulse rate 125 beats a minute, respiratory rate 65 a minute. No response to the intravenous transfusion of 2 pints of saline. Premedication, atropine 0.5 mg.

Anaesthesia was induced with nitrous oxide, oxygen and halothane. Three pints of glucose-saline were administered intravenously during the next 15 minutes. The skin became warm, dry, and pink and the blood-pressure, after an initial fall to 70 mm Hg systolic, rapidly increased to 130 mm Hg systolic and the pulse rate dropped to 100 beats a minute. A laparotomy was then performed under halothane-oxygen anaesthesia and the gastric perforation repaired, a further 2 pints of glucose-saline being administered. The blood pressure varied between 110 and 140 mm Hg systolic during the operation and increased to 150 mm Hg systolic immediately afterwards. Recovery was uneventful.

CASE 3. Female, 81 years. Right femoral hernia strangulated for 7 days. Chronic bronchitis. Collapsed, dehydrated, cyanotic, respiratory rate 45 a minute, pulse rate 135 beats a minute, peripheral vasoconstriction, tongue dry and shrunken, blood pressure 110/80 mm Hg (known to have been 230/130 mm Hg before the intestinal strangulation). Premedication, atropine 0.5 mg.

Anaesthesia was induced with nitrous oxide, oxygen, and halothane. Three pints of glucose-saline were

administered intravenously (forearm vein) during the next 15 minutes. The skin became pink and warm and the blood pressure increased to 130 mm Hg systolic. Anaesthesia was then maintained with halothane and oxygen and, during the next 75 minutes, the hernia was reduced and repaired and 3 inches of gangrenous intestine excised followed by an end-to-end anastomosis. A further 2 pints of glucose-saline were administered during the operation. At the end of the operation the blood pressure was 150 mm Hg systolic, the pulse rate 110 beats a minute, the respiratory rate 30 a minute, and the tongue had become moist and of normal size. Consciousness returned in 10 minutes and the blood pressure gradually increased to 170/100 mm Hg during the next 3 hours. Recovery was uneventful.

CASE 4. Male, 62 years. Right renal tumour. Heart and lungs normal. Blood pressure 190/110 mm Hg. Premedication, pethidine 50 mg and promethazine 50 mg.

Anaesthesia was induced with thiopentone 250 mg (with atropine 0.5 mg) and an endotracheal tube inserted during suxamethonium paralysis. Anaesthesia maintained with halothane and oxygen, no relaxants or other supplements being necessary. The blood pressure after premedication was 150/100 and dropped to 110/70 mm Hg during halothane anaesthesia. Spontaneous respiration persisted throughout with a respiratory rate of 30 a minute. Before induction the pulse rate was 85 beats a minute, and dropped to 70 beats a minute when anaesthesia was established with halothane.

Exploration of the right renal area revealed a large retroperitoneal neoplasm investing and infiltrating the kidney and several large blood vessels including the inferior vena cava and the right common iliac artery and vein. Fifty minutes after the start of the operation and during an attempt to mobilize the tumour the right common iliac artery and vein were torn; torrential haemorrhage followed and the blood pressure immediately dropped to zero in the arms but a feeble pulse was palpable in the carotid artery at 70 beats a minute. The haemorrhage was controlled by direct pressure on the bleeding area. During the next 10 minutes 1 pint of saline and 2 pints of blood were administered intravenously and caused the blood pressure to rise to 90 mm Hg systolic. An attempt was then made to apply haemostatic ligatures but this resulted in more haemorrhage and the blood pressure again dropped to zero; a further 2 pints of blood and 1 pint of dextran restored the blood pressure to 100 mm Hg systolic in 8 minutes. Attempts to control the haemorrhage occupied 65 minutes during which time 10 pints of blood, 3 pints of glucose-saline and 3 pints of dextran were administered intravenously. The entire transfusion was administered through a vein on the dorsum of the right hand, using the standard giving-set and a Martin's pump. Whenever necessary the hypertensive response to the transfusion was increased by diminishing the depth of anaesthesia and by 5 mg doses of methoxamine (total dose 20 mg)—this drug is particularly effective in counteracting any tendency to pooling of blood in the dependent parts of the body. Throughout the operation the pulse and respiratory rates remained unchanged at 70 beats a minute and 30 a minute respectively, and the skin remained warm and dry. During the more critical hypotensive periods, none of which lasted more than 5 minutes, cyanotic patches appeared on the dependent parts of the body, and the uppermost areas became very pale; restoration of the blood pressure caused the skin to regain its normal pink appearance immediately.

The operation was completed in 3¼ hours. The patient recovered consciousness 15 minutes later and was returned to the ward in good condition, his brachial blood pressure being 190/110 mm Hg and pulse rate 65 beats a minute. At the conclusion of the operation pulsation was absent in both femoral arteries and did not return subsequently. The patient remained in good condition for 24 hours after the operation, fully conscious and rational, his blood pressure remaining around 150/100 mm Hg. A few hours later he died rather suddenly from causes unrelated to anaesthesia.

CASE 5. Male, 58 years. Obese. Left hypernephroma, 20 cm approximately in diameter. Blood pressure 170/90 mm Hg. Premedication pethidine 50 mg with atropine 0.6 mg.

Anaesthesia was induced with thiopentone 300 mg and the patient intubated during suxamethonium paralysis. Anaesthesia was then maintained with halothane-oxygen with adequate spontaneous respiration and muscular relaxation throughout. With halothane anaesthesia the blood pressure settled at 100 mm Hg systolic with a pulse rate of 84 beats a minute. A large hypernephroma was mobilized without difficulty, During the removal of the tumour the haemostatic clamp slipped from the atherosclerotic renal artery with the immediate loss of from two to three pints of blood before the clamp was satisfactorily reapplied. The radial blood pressure immediately became unrecordable and the carotid pulse rate dropped to 60 beats a minute. Methoxamine 10 mg was injected intravenously (per saline intravenous drip already in situ) followed by 1 pint of dextran and 5 minutes later the blood pressure was 75 systolic and the pulse rate 70 beats a minute. Two pints of blood and 1 pint of saline were administered during the next 15 minutes, using a vein on the dorsum of the left hand with a standard giving-set and the systolic blood pressure promptly increased to 120 mm Hg, the pulse rate remaining unchanged at 70 beats a minute. At the end of the operation, which lasted 90 minutes, the blood pressure was 150/100 mm Hg, the pulse rate 80 beats a minute, and full consciousness returned 30 minutes later, the skin remaining warm, dry, and pink. No subsequent drop in blood pressure occurred and the patient made a complete and uneventful recovery.

CONCLUSION

Halothane has provided strong, if not conclusive, evidence in favour of the concept that vasoconstriction is an undesirable consequence of trauma or haemorrhage in the subject under medical care. Constriction of the peripheral vessels in response to haemorrhage or other stimuli is undoubtedly designed by nature as a protective

mechanism but it is difficult to perceive how this reaction fits into the efficient management of patients undergoing elective or emergency surgical operations in conditions where adequate facilities are available for the maintenance of blood volume by transfusion methods. It should not be forgotten that pain perception is also a highly important defence against injury but no one would suggest that it is in any way necessary for the survival of patients undergoing surgical treatment.

The abolition of the vasoconstrictive reaction to injury, although of fundamental importance in the control of surgical shock, carries serious and perhaps dangerous risk to the patient if it is not fully realised that the sensitivity of the patient to the cerebral and cardiac complications of hypovolaemia and hypotension are increased. Unlike all the other vasoplegic drugs introduced into clinical practice, however, halothane provides a vasoparesis which is completely under the control of the anaesthetist and which can be varied momentarily in either direction by altering the concentration of the inhaled vapour. The restoration of vasomotor tone, when it becomes necessary, can be effected so rapidly either by stopping the administration of halothane or by giving methoxamine that the threat to the cerebral and coronary circulation is reduced to a minimum, if not completely eliminated. The unusually high proportion of oxygen which is administered with the drug without impairing its narcotic and relaxant properties is undoubtedly a major factor in the increased tolerance to generalized vasodilatation.

The necessity for narcotic and relaxant supplementation of the other ganglioplegic methods greatly increased the dangers of these methods, survival from the effects of many of the conventional narcotics and relaxants being dependent to a large extent on the integrity of the vasomotor system and the efficiency of the respiratory movements. Halothane, on the other hand, not only provides rapidly reversible narcosis and muscular relaxation but preserves the vital function for which no complete substitute has been found and which is the most satisfactory index of anaesthetic dosage—spontaneous respiration.

It can be concluded that halothane is an efficient anaesthetic agent which ensures the immediate effectiveness of resuscitative measures, thereby eliminating the dangers of peripheral circulatory collapse during surgery. The only problem which it has presented has been the difficulty in finding explanations of its unusual and beneficial effects. The clinician is strictly limited in the means to be adopted in investigating these effects but it should not be forgotten that, in the final analysis, the only satisfactory criterion of the value of any anaesthetic agent is the condition of the patient throughout and after the operation—and in this respect halothane has not been found wanting.

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